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Journal of Occupational Medicine

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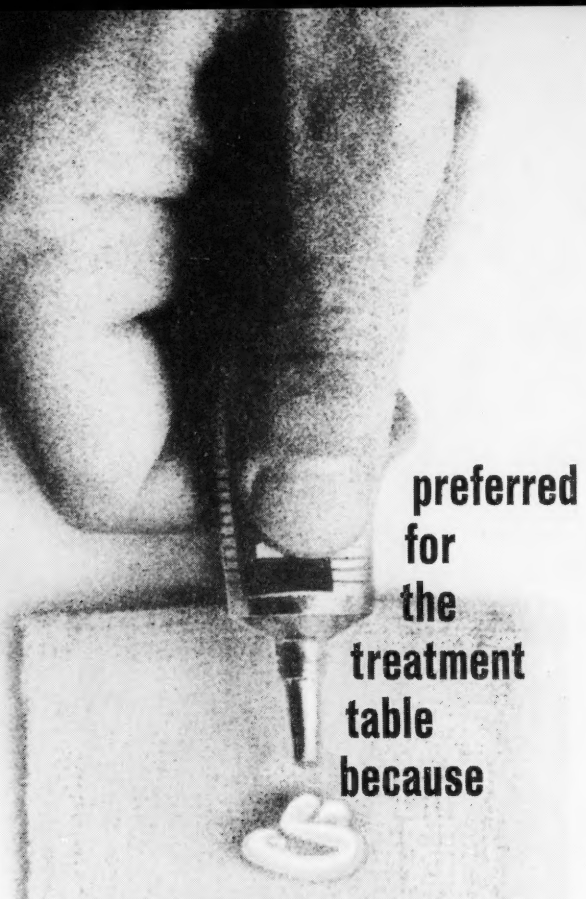

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The Industrial Medical Association was organized in 1915 as the American Association of Industrial Physicians and Surgeons. Its first annual meeting was held the following year. In 1951 the present name was adopted.

The purposes of the organization as stated in the certificate of incorporation (not-for-profit) are:

"The object of this Association will be to foster the study and discussion of the problems peculiar to industrial medicine and surgery; to develop methods adapted to the conservation of health among workers in the industries; to promote a more general understanding of the purposes of the medical care for employees; and to unite into one organization members of the medical profession specializing in industrial medicine and surgery for their mutual advancement in the practice of their profession."

Presently, the membership includes more than 4000 physicians in the United States, Canada, Latin America, and other parts of the world. Physicians "who have an interest in Industrial Medicine" may apply for membership; specialization in this field is not essential. Regionally, the Industrial Medicine Association has 15 Component Societies in the United States. Most Association members carry their membership through one of the component groups.

The Journal of Occupational Medicine, owned and published by the Industrial Medical Association, is sent monthly to each member as one of the advantages of membership.

The annual business meeting and convention is held in the spring. Since 1945, the convention has been held concurrently with the meetings of four other organizations having related interests—American Industrial Hygiene Association, American Conference of Governmental Industrial Hygienists, American Association of Industrial Nurses, Inc., American Association of Industrial Dentists. This combined meeting is known as the Industrial Health Conference.

The Occupational Health Institute, Inc., is a non-profit educational organization created by the Industrial Medical Association to promote the cause of health in industry. Since 1951, the Occupational Health Institute has conducted the program of evaluation, approval and certification of Medical Services in Industry, on the basis of standards established by the Standards Committee of the Industrial Medical Association. This program was conducted by the American College of Surgeons for many years until its transfer to the Association.

The Association's headquarters office serves as a focal point for the Association's activities and through its coordination of information regarding industrial health problems encountered throughout the country, it offers invaluable assistance to members on a host of specific subjects.

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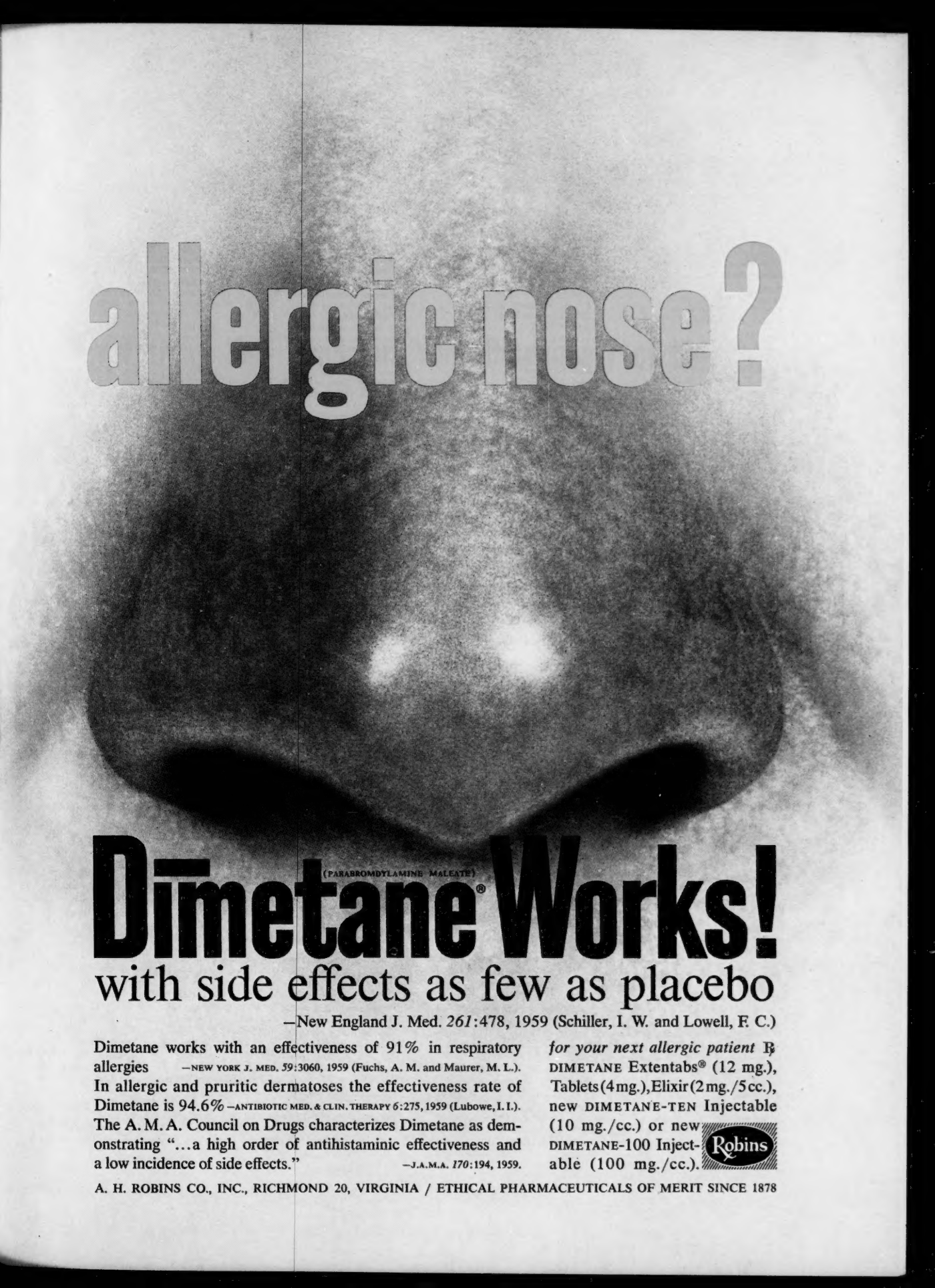

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An important function of the District Counselor is to serve in a liaison capacity with the Component Society of the Industrial Medical Association in his area. The District Counselor also is concerned with regional trends in industrial medical practice and in legislation bearing upon medical service in industry. He is ready to assist any physician with questions or problems.

In promoting the cause of industrial medicine, many District Counselors work with the industrial health committees of their state medical societies, they participate in teaching programs at hospitals or medical schools, and serve as speakers at meetings of groups that express interest in occupational health. Throughout these activities, the District Counselor attempts to stimulate membership in the Industrial Medical Association by acquainting others with the organization's purposes and facilities.

By keeping in close contact with members in his area, the District Counselor gains a familiarity with their work which enables him to make recommendations to the Association's officers and committees regarding those qualified for various positions or honors. He recommends members for committee work, and for fellowship, and recommends fellows for consideration for elective offices in the Association. He also recommends possible recipients for the awards presented at the annual meeting of the Association—the Knudsen Award, the Health Achievement in Industry Award, the Meritorious Service Award and the Merit in Authorship Award.

Many District Counselors also serve as Regional Consultants for the Occupational Health Institute, the educational affiliate of the IMA.

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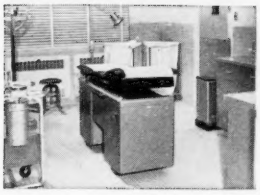

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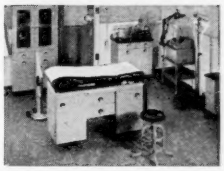

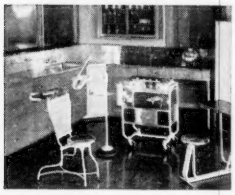

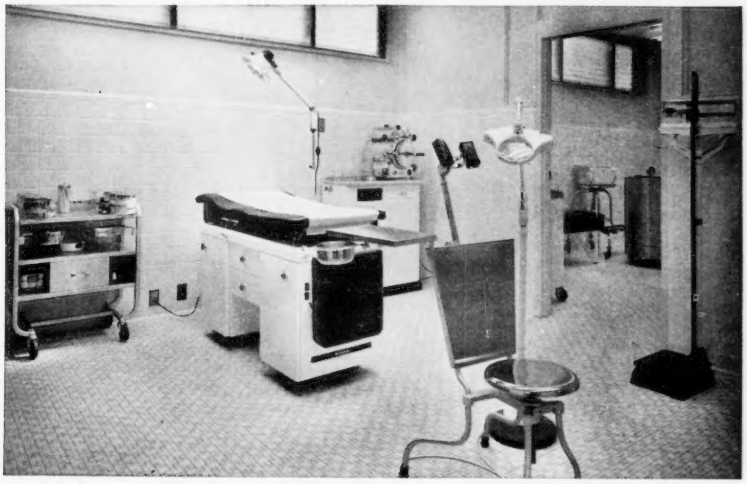

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Journal of Occupational Medicine

A Study of Mass Influenza Inoculation in a Large Industry

Clyde C. Greene Jr., M.D., and Glen T. Beaver, B.S., San Francisco, Calif.

EPIDEMICS have traditionally caused costly losses in business and industry through lost time and inefficiency of employees. This has been particularly true of a service type business or a public utility, which must function on a continuous basis. In 1957, with Asian influenza becoming epidemic on almost a worldwide basis, The Pacific Telephone and Telegraph Company decided to offer, at company expense, influenza immunization to its 93,000 employees. At that time plans were made for a follow-up survey about six months later. Since we were unable to determine scientifically the effectiveness of our immunization program, we selected this technique of employee evaluation. While we were aware of the defects inherent in this type of a study, we believed that such an employee survey would provide industry and the medical profession with useful though nonscientific information about influenza immunization. Accurate records were kept as to the costs and quantity of vaccine used.

Procedure

During the months of August and September, 1957, a total of 56,818 employees, or 61% of the entire force of 93,288, requested and received influenza vaccination. These injections were administered by company medical personnel in the larger cities, and by local medical consultants and their nurses in all other localities. The program was offered throughout the company's operating territory in California, Washington, Oregon, Nevada, and a portion of Idaho.

An injection of 1 cc of monovalent Asian Strain vaccine, containing 200 CCA (chicken-cell agglutination titer) units per cubic centimeter, was given subcutaneously to each employee requesting an inoculation. The more potent vaccine now used (generally 400 CCA units per cubic centimeter) was not then available.

In April, 1958, we distributed a questionnaire, through lines of supervision, to the 88,079 employees who were then on the payroll. The purpose was (1) to determine a measure of the effectiveness of the vaccine and (2) to determine the attitude of employees toward the program. While supervisors were advised not to "force" employees to complete the questionnaire, we have reasonable assurance that most nonresponding employees were in three categories of "on vacation," "out of town," "sick," or "missed through supervisor error." None of these categories should be overly weighted with either inoculated or noninoculated employees.

The questionnaire was self-administered. Employees were instructed not to sign their names on the theory that anonymity would encourage frankness in responses, particularly those involving attitudes and sickness absence experience. The questions were designed to cover all illnesses that employees would ordinarily consider as "influenza." No attempt was

Dr. Greene is General Medical Director and Mr. Beaver is General Statistician, The Pacific Telephone & Telegraph Company.

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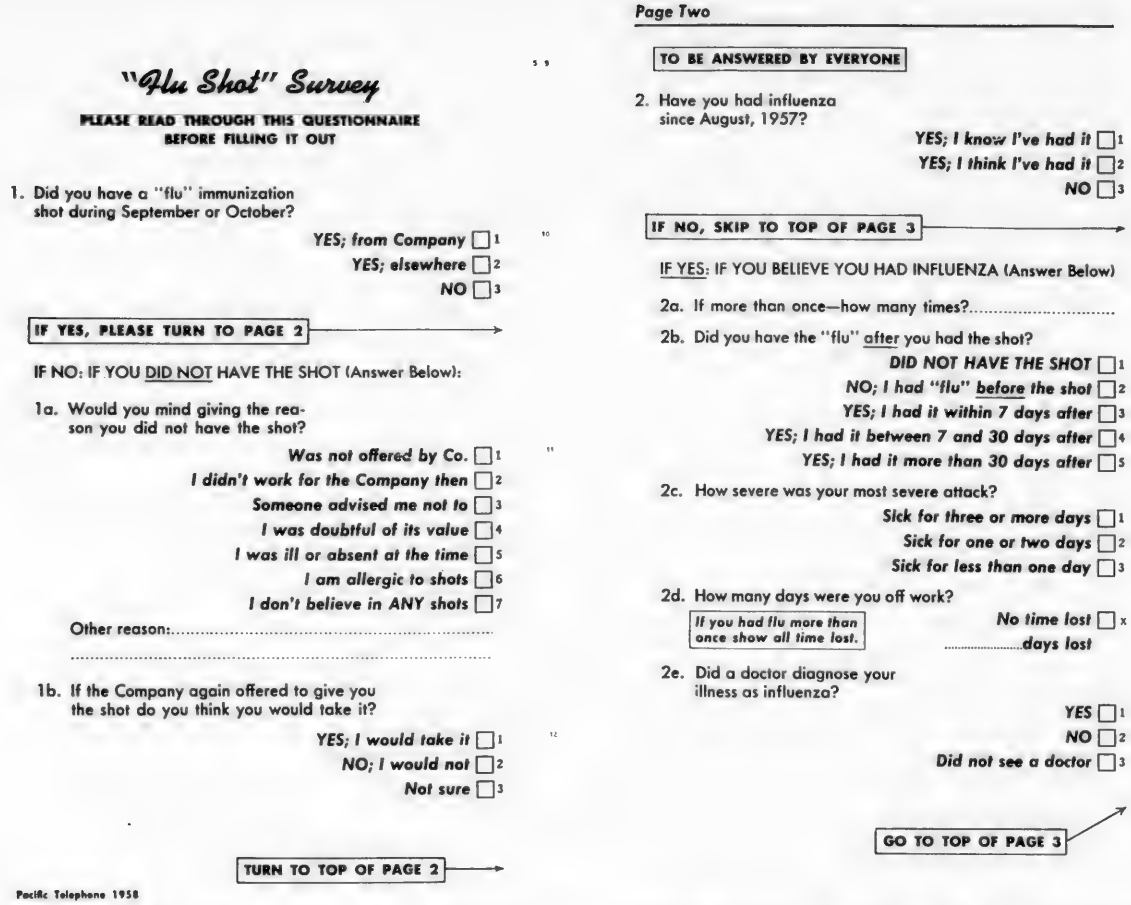


"Flu Shot" Survey

PLEASE READ THROUGH THIS QUESTIONNAIRE BEFORE FILLING IT OUT

1. Did you have a "flu" immunization shot during September or October?

YES; from Company ☐1
YES; elsewhere ☐2
NO ☐3

IF YES, PLEASE TURN TO PAGE 2

IF NO: IF YOU DID NOT HAVE THE SHOT (Answer Below):

1a. Would you mind giving the reason you did not have the shot?

Was not offered by Co. ☐1
I didn't work for the Company then ☐2
Someone advised me not to ☐3
I was doubtful of its value ☐4
I was ill or absent at the time ☐5
I am allergic to shots ☐6
I don't believe in ANY shots ☐7

Other reason:.....

.....

1b. If the Company again offered to give you the shot do you think you would take it?

YES; I would take it ☐1
NO; I would not ☐2
Not sure ☐3

TURN TO TOP OF PAGE 2

Pacific Telephone 1958

Page Two

TO BE ANSWERED BY EVERYONE

2. Have you had influenza since August, 1957?

YES; I know I've had it ☐1
YES; I think I've had it ☐2
NO ☐3

IF NO, SKIP TO TOP OF PAGE 3

IF YES: IF YOU BELIEVE YOU HAD INFLUENZA (Answer Below)

2a. If more than once—how many times?.....

2b. Did you have the "flu" after you had the shot?

DID NOT HAVE THE SHOT ☐1
NO; I had "flu" before the shot ☐2
YES; I had it within 7 days after ☐3
YES; I had it between 7 and 30 days after ☐4
YES; I had it more than 30 days after ☐5

2c. How severe was your most severe attack?

Sick for three or more days ☐1
Sick for one or two days ☐2
Sick for less than one day ☐3

2d. How many days were you off work?

If you had flu more than once show all time lost.

No time lost ☐x
.....days lost

2e. Did a doctor diagnose your illness as influenza?

YES ☐1
NO ☐2
Did not see a doctor ☐3

GO TO TOP OF PAGE 3

made to separately identify Asian strain influenza.

Evaluation of the Data

In order to evaluate the vaccine effectiveness data included in this paper, the following points should be kept in mind:

1. The inoculations were designed to reduce only the incidence and severity of Asian Strain influenza, and were of a lower dosage than presently recommended.

2. The inoculated and noninoculated groups were self-selected. For policy reasons, we could not preselect the groups, although this would have been desirable. While self-selection can introduce bias, we believe that such bias was nominal in this study.

3. The "influenza" cases reported by employees were largely self-diagnosed, with a lapse of about seven months between the administration of the vaccine and the distribution of the questionnaire to the employees.

4. Even those cases of influenza reported as confirmed by a physician are open to some question with regard to specific viral etiology. Only complex laboratory tests will unconditionally confirm the diagnosis of influenza.

In view of these four points, any estimate of the effectiveness of immunization must be made on a comparative basis between the inoculated and noninoculated groups, rather than in terms of the total number of cases. With the large number of persons covered in this survey, it would seem reasonable to assume that approximately the same degree of bias and errors in reporting would exist in each group.

This is a statistical paper based upon the unverified statements of a large group of employees. No scientific controls or medical tests were involved. It is hoped, however, that the data collected may be of value to industry and the medical profession, as few studies of this size have been attempted.

Response to Questionnaires

A total of 76,136 employees, or 86.4% of the 88,079 employees on the payroll at the time the study was made, returned usable questionnaires. Of these, 64.8%, or 49,307, said that they had been inoculated. This 64.8% com-

Page Three

IF YOU DID NOT HAVE THE SHOT, TURN TO PAGE 4 →

IF YOU DID HAVE THE SHOT (Answer Below)

3. In general, do you believe the shot did you any good?
   - YES; I think it did me some good ☐ 1
   - NO; I think it was harmful ☐ 2
   - I think it made no difference ☐ 3

3a. Did you have any reaction to the shot?
   - Rash-Hives (Allergic Reaction) ☐ 1
   - Sore arm for a few hours ☐ 2
   - Painful arm for several days ☐ 3
   - Chills-Fever ☐ 4
   - Headaches ☐ 5
   - Other reaction ..... Stomach Sickness ☐ 6
   - ..... NO REACTION ☐ 7

IF NO REACTION, SKIP TO PAGE 4 →

IF YOU DID HAVE A REACTION (Answer Below)

3b. How long after the shot did you first feel the reaction?
   - Same day ☐ 1
   - Next day ☐ 2
   - Later than next day ☐ 3

3c. Did you see a doctor about this reaction?
   - YES; doctor at Company ☐ 1
   - YES; other doctor ☐ 2
   - NO ☐ 3

If yes: (If you saw a doctor) Did he say that the reaction was from the "flu" shot?
   - YES ☐ 1
   - NO ☐ 2
   - Did not see doctor ☐ 0

3d. Did you lose any time from work because of this reaction?
   - No time lost ☐ x
   - .....days lost

TURN TO PAGE 4 →

Page Four

TO BE ANSWERED BY EVERYONE

4. Do you feel that Telephone Company Programs of this type are beneficial or not beneficial to employees?
   - Are beneficial ☐ 1
   - Are not beneficial ☐ 2
   - No opinion ☐ 3

Please give us any other comments you may have on this general subject:

.....

.....

.....

.....

.....

.....

BE SURE TO CHECK THE FOLLOWING:

AREA:
- Washington-Idaho ☐ 1
- Oregon ☐ 2
- Northern Calif. ☐ 3
- Southern Calif. Region ☐ 4
- Nevada ☐ 5
- Genl. Hq. or Calif. Admin. ☐ 6

AGE:
- Under 21 ☐ 1
- 21-40 Yrs. ☐ 2
- 41-60 Yrs. ☐ 3
- Over 60 ☐ 4

DEPARTMENT:
- Plant ☐ 1
- Traffic ☐ 2
- Commercial ☐ 3
- Engineering ☐ 4
- Accounting ☐ 5
- Other ☐ 6

SEX:
- Man ☐ 1
- Woman ☐ 2

I WORK IN: ..... (CITY)

After you finish, please put this questionnaire in the envelope. Seal it and return it to your supervisor.

THANK YOU

pares quite closely with the 61% of the total employees who actually received the vaccine seven months before and indicates that nonrespondents were not unduly weighted in either the inoculated or the noninoculated group.

Of the 26,829 employees who said that they had not been inoculated, 17,210, or 64.1%, said they had refused for such reasons as, "I was doubtful of its value," "allergic to inoculations," "allergic to eggs," "advised not to," or "don't believe in any shots." Another 9,185, or 34.2% of the employees, said that they had missed the opportunity of inoculation through illness, through other absence, or because they were not on the payroll when the vaccine was administered. About two-thirds of those missing inoculation said that they would accept the vaccine if it were offered again. Only 14% of those refusing inoculation said they would accept if offered again.

Incidence of Influenza

The employee group receiving vaccine from the Company* reported 7.7% fewer cases of influenza than the noninoculated group. This is a statistically significant difference. The employees studied covered both sexes, most age groups, wide geographical dispersion, and variation in economic status. If they are considered as a reasonable sample of the over-all industrial population, the application of sampling theory statistics shows that the difference in incidence rates reported is almost 23 times the standard error of the difference between them. Such a difference can almost certainly not arise by chance. To a lesser degree, our employee force can be considered as a cross section of the adult civilian population in the Western states.

The difference in incidence of influenza between noninoculated and inoculated women was greater (9.3%) than for men (5.0%) as shown in Chart I.

As stated previously, the influenza reported by employees was largely self-diagnosed. All material in this paper is based on what the

*While data are available for 2,154 employees who said they had received inoculations elsewhere, it was decided to discard responses from these employees on the basis that we did not know what type of vaccine was given to them. All subsequent data in this paper exclude these 2,154 employees.

employees reported, with no attempt made to edit or "second guess" these reports. However, at this point, one editorial observation will be made. If data from employees who reported less than one day of sickness are eliminated (employees who probably did not have influenza at all) the inoculated group experienced 11.6% less influenza than the noninoculated group.

Because of the incubation period of influenza, cases reported as occurring less than seven days after inoculation were arbitrarily classified as "no influenza after inoculation."

Analysis of differences in incidence of influenza between inoculated and noninoculated employees by age groups showed that the noninoculated lower age groups (under 21 and 21-40) reported a considerably higher incidence than the inoculated. These differences were as follows: for women under 21, 16.3%; for women 21-40, 10.0% for men under 21, 12.7%; and for men 21-40, 6.4%. Little difference was reported in the 41-60 year group in either sex, and in the 60 year and over group, inoculated men and women reported a slightly higher incidence of influenza (Chart II).

Severity of Influenza

Average days lost from work may be considered as a measure of the severity of the influenza cases reported. Noninoculated employees who reported that they had influenza lost 17.9% more days from work than inoculated employees. This difference was much greater (30.3%) for men and less (8.0%) for women (Table I).

Percent difference in lost time by age was relatively constant between noninoculated and inoculated women (8.1%-10.8%). This difference was greater for men, ranging from 57.8% for men in the under 21 group to 23.9% in the 41-60 year group.

Lost time was reported by 2,782, or 13.2%, of inoculated men and 4,213, or 18.0%, of inoculated women, as contrasted to 1,782, or 18.2%, of noninoculated men and 3,714, or 24.0%, of noninoculated women.

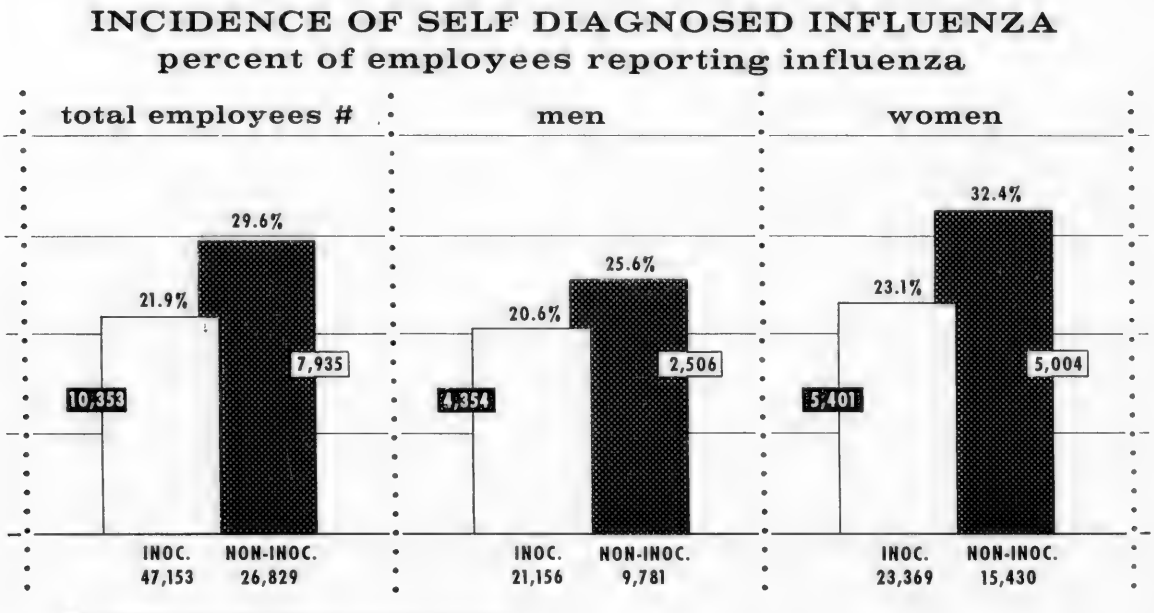
Some additional data on the severity of the influenza reported are contained in Tables II, III, and IV, which are based upon the 10,353 inoculated and 7,935 noninoculated employees who reported getting influenza.

Accuracy of Reporting

In a study such as this, where self-selection of vaccine or no vaccine exists and where self-diagnosis and memory are involved, there is rightfully a question as to whether there may be bias in the groupings and bias and error in the responses.

While this question cannot be unconditionally answered in regard to this study, Table V indicates consistency of reporting between the inoculated and noninoculated groups in regard to those who "knew I had influenza," "thought I

CHART I



Includes responses where sex not indicated.

Table I—Average Days Lost Time Reported by Employees Who Reported Having Influenza

Reporting Group	Noninoculated Employees Reporting Influenza		Inoculated Employees Reporting Influenza		Difference In Av. Days Lost	% Difference
	No.	Av. Days Lost	No.	Av. Days Lost		
	(A)	(B)	(C)	(D)	(E) = (B) − (D)	(F) = $\frac{(E)}{(D)} \times 100$
All employees	7,935	2.90	10,353	2.46	0.44	17.9
Men	2,506	2.54	4,354	1.95	0.59	30.3
Women	5,004	3.11	5,401	2.88	0.23	8.0
By age groups						
Men under 21	237	2.32	155	1.47	0.85	57.8
21 to 40	1,678	2.39	3,075	1.79	0.60	33.5
41 to 60	525	3.11	1,013	2.51	0.60	23.9
over 60	42	3.31	69	2.55	0.76	29.9
Women under 21	1,420	2.81	955	2.60	0.21	8.1
21 to 40	2,706	3.08	3,239	2.78	0.30	10.8
41 to 60	785	3.71	1,095	3.35	0.36	10.7
over 60	40	4.45	51	4.10	0.35	8.5

had influenza," who consulted a physician and whose cases were diagnosed as influenza by a physician.

However, it appears that the inoculated group probably erroneously self-diagnosed influenza to a greater extent than the noninoculated group. This is based on the assumption that cases of less than one day's sickness were probably not influenza. As shown under "Duration of Sickness Reported," in Table III, 55.2% of the inoculated group reporting influenza claimed to have been sick less than one day, as contrasted to 27.6% of the noninoculated group.

Reaction to Inoculations

Of the 47,153 employees inoculated by the company, 13,123, or 27.8%, reported reactions severer than "a sore arm for a few hours." Lost time from work was reported by 1,465, or 11.2%, of those reporting reactions (3.1% of those inoculated). Total lost time reported amounted to 3,271 days, which equates to an average of 2.2 days per lost time case, or about a half-hour per employee inoculated.

There were no fatalities due to reactions. Lost time in excess of one week was reported by 80 employees.

CHART II

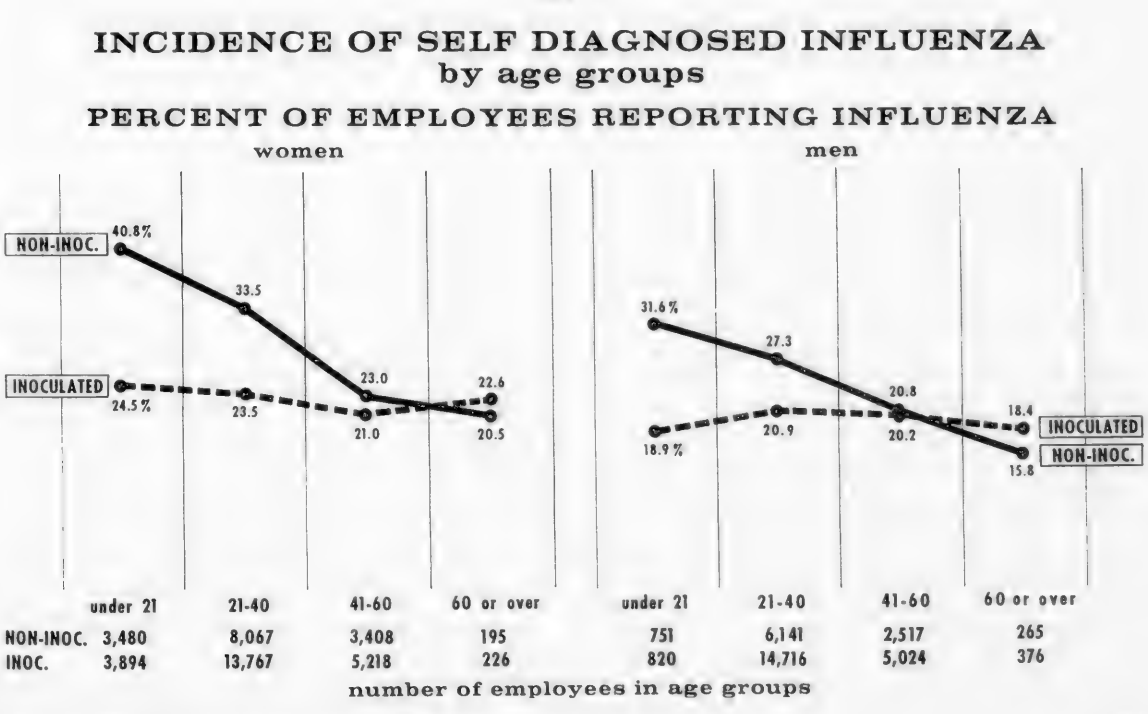


Table II—Number of Times Employee Had Influenza Between August, 1957, and April, 1958

	Inoculated Employees		Noninoculated Employees	
	No. Times	% of Total	No. Times	% of Total
Once	8,635	83.4	6,710	84.6
Twice	1,386	13.4	986	12.4
3 or more times	332	3.2	239	3.0
Total	10,353	100.0	7,935	100.0

Table III—Duration of Severest Attack

	Inoculated Employees		Noninoculated Employees	
	No.	% of Total	No.	% of Total
Sick 3 or more days	400	3.9	713	9.0
Sick 1 or 2 days	3,468	33.5	4,845	61.1
Sick less than 1 day	5,721	55.2	2,192	27.6
Not indicated	764	7.4	185	2.3
Total	10,353	100.0	7,935	100.0

Table IV—Days Lost From Work

	Inoculated Employees		Noninoculated Employees	
	No.	% of Total	No.	% of Total
No lost time	2,102	20.3	1,333	16.8
One day	1,351	13.0	800	10.1
Two days	1,901	18.4	1,275	16.1
Three days	1,361	13.1	936	11.8
Four days	814	7.9	647	8.1
Five days	902	8.7	892	11.2
Six or more days	1,082	10.5	1,229	15.5
Not indicated	840	8.1	823	10.4
Total	10,353	100.0	7,935	100.0

Employee Attitude Toward Inoculations

Employees who had been inoculated were asked if they "believed the inoculation did you any good." Most employees (78.6%) said, "I think it did me some good." Even those employees who reported reactions or influenza were generally favorably inclined toward the inoculations, as indicated in Table VII.

All employees were also asked if they felt that "programs of this type are beneficial or not beneficial to employees." The response to this question was very favorable, as shown in Table VIII.

Cost and Savings Considerations

The data obtained from this study indicate that the inoculated group of employees experienced not only a lower incidence of influenza than the noninoculated group but also had experienced less lost time when affected by influenza.

Let us assume that the inoculated group would have had the same incidence and lost time experience as the noninoculated group if inoculations, had not been given. On the basis of this assumption, the inoculated group would have had more lost time than actually experienced. The cost of this additional lost time can be considered as a measure of what the influenza inoculation program saved the company in lost time costs.

These savings were considerably more than

Table V—Reported Data

	Inoculated Group		Noninoculated Group	
	Number	% of Employees in Group	Number	% of Employees in Group
Employees in group	47,153	100.0	26,829	100.0
Employees reporting influenza	10,353	21.9	7,935	29.6
"Knew" they had influenza	5,816	12.3	4,508	16.8
"Thought" they had influenza	4,537	9.6	3,427	12.8
Consulted M.D.	4,804	10.2	4,213	15.7
M.D. diagnosed influenza	3,692	7.8	3,448	12.8

Of the 13,123 reported reaction cases, 12,515, or 95.4%, were self-diagnosed. A physician was consulted by 860, or 6.5%, of the 13,123 employees reporting reactions. Of these 860 cases, 608, or 70.7%, were diagnosed by the physician as a reaction to the inoculation.

The onset of reactions was reported as follows: same day as inoculation, 7,727, or 58.9%; next day, 3,164, or 24.1%; later than next day, 1,176, or 9.0%. Of employees reporting reactions 1,056, or 8.0%, did not state when the reaction occurred.

Types of reactions reported are indicated in Table VI.

Table VI—Reaction Symptoms Reported by Inoculated Employees

Symptom	No. of Reactions	% of Total Reactions
Rash-hives	250	1.3
Painful arm*	6,354	31.9
Chills-fever	5,154	25.9
Headache	3,618	18.1
Gastrointestinal upset	2,724	13.7
Other	1,823	9.1
Total	19,923	100.0

While 13,123 employees reported reactions, the total of 19,923 is due to the reporting of more than one symptom by some employees.

*Does not include 17,769 employees who reported "sore arm for a few hours."

Table VII—Response to Question "Do You Believe the Inoculation Did You Any Good?" (Asked of All Inoculated Employees)

Response	All Employees		Employees Reporting Infl.		Employees Reporting no Infl.		Employees Reporting Reaction	
	No.	% of total	No.	% of total	No.	% of total	No.	% of total
Think it did me some good	37,067	78.6	6,474	62.5	30,593	83.1	9,701	73.9
Think it was harmful	1,051	2.2	612	5.9	439	1.2	787	6.0
Made no difference	6,606	14.0	2,664	25.7	3,942	10.7	2,110	16.1
Don't know	333	0.7	79	0.8	254	0.7	99	0.8
No answer	2,096	4.5	524	5.1	1,572	4.3	426	3.2
Total	47,153	100.0	10,353	100.0	36,800	100.0	13,123	100.0

Table VIII—Response to Question "Do You Feel That Programs of This Type Are Beneficial or Not Beneficial to Employees?" (Asked of all Employees)

Response	All Employees		Inoculated Employees		Noninoculated Employees	
	No.	% of total	Report Infl.	Report no Infl.	Report Infl.	Report no Infl.
Beneficial	66,316	89.6%	89.1%	96.6%	84.6%	78.4%
Not beneficial	736	1.0	1.5	0.3	1.0	2.1
No opinion	6,111	8.3	8.1	2.6	13.0	17.4
No answer	819	1.1	1.3	0.5	1.4	2.1
Total	73,982	100.0	100.0%	100.0%	100.0%	100.0%

the cost of the inoculation program, as shown below:

Incidence rate of noninoculated employees was 7.7% higher than inoculated employees.

47,153 (inoculated employees) × 7.7(%) = 3,631 additional cases if no inoculations had been given.

3,631 cases @ 2.90 days lost time per case (lost time rate of noninoculated employees) = 10,530 additional days lost time

Lost time of noninoculated employees who reported influenza was 0.44 days more than inoculated employees who reported influenza.

10,353 inoculated employees who reported influenza × 0.44 = 4,555 additional days lost time

Total additional days lost time in inoculated group if no inoculations had been given 15,085

Approximately 80% of sickness absence is paid absence (depends upon length of service of employee)

0.80 × 15,085 = 12,068 paid days @ $20.40 (Aver. wage cost Sept. 1957) = $246,187

Less lost time due to reactions: 3,271 paid days @ $20.40 = −66,728

Gross saving $179,459

Less cost of inoculations −51,000

Net savings due to inoculation program $128,459

This computation does not include any measurement of the savings to employees of suffering, inconvenience and medical expense.

Conclusions

Analysis of data furnished by 76,136 employees with respect to influenza inoculation permits the following general observations:

1. Inoculated employees reported a lower incidence of influenza (7.7%) than noninoculated employees. This is a significant difference, and suggests to industry that such an immunization program is effective for the control of employee absence resulting from epidemic influenza.

In the employee group reporting one or more days of sickness, (those who probably really had influenza) inoculated employees reported 11.6% less influenza than noninoculated employees.

2. Inoculated employees who claimed to have

had influenza reported less lost time (17.9%) than noninoculated employees who claimed to have had influenza.

3. Three out of four employees receiving the inoculation felt that it did them some good. Interestingly 73.9% of the employees reporting a reaction to the vaccine felt that the inoculation "did some good."

4. Nine out of ten employees from whom data was received felt that inoculation programs of this type are beneficial.

5. The cost of the inoculation program, including the cost of self-diagnosed vaccine reactions, was more than offset by reduced absenteeism in the company.

(The authors' address is The Pacific Telephone & Telegraph Company, 140 New Montgomery St., San Francisco 5, Calif.)

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- Graduate Training in Occupational Medicine—The In-Plant Component—Paul J. Whitaker, M.D. (July, 1960).
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Noise and Hearing Loss (Topical Review)—Lieut. Cmdr. Norbert E. Rosenwinkel (MC) U.S.N., Kenneth C. Stewart, M.S., and Leo G. Doerfler, Ph.D.: Part I (Jan., 1959); Part II (April, 1959), and Part III (July, 1959).

Certification in Occupational Medicine: I. Backgrounds and Policies Involved in Certification—Robert A. Kehoe, M.D.; II. Nature and Objectives of the Specialty—James H. Sterner, M.D.; III. Qualifications of the Certified Specialist—A. G. Kammer, M.D. (May, 1959).

Occupational Skin Problems (Topical Review)—Raymond R. Suskind, M.D.: I. Mechanisms of Dermatologic Response (Jan., 1959); II. Methods of Evaluation for Cutaneous Hazards (Feb., 1959); III. Case Study and Diagnostic Appraisal (April, 1959).

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- Editorial—Heart Disease and Employment (March, 1959).

Present Position of Government in Occupational Health—Seward E. Miller, M.D. (Jan., 1959).

DTPA—Effectiveness in Removing Internally Deposited Plutonium from Humans

W. D. Norwood, M.D., Richland, Wash.

IT SEEMS obvious that there will be a continuing increase in the potential for exposure to internally deposited radioisotopes with the expanding use of such materials in defense, medicine, and industry. This has accelerated the search for more effective agents to remove the dangerous isotopes from the body.

Plutonium (Pu^{239}) is one of the most hazardous of such isotopes because of its deposition within the body near the active elements of the bone and marrow, its energetic alpha emissions, and its long effective half-life within the body (118 years).[1] This article discusses the effectiveness, dosage, and safety of trisodium diethylenetetraminepentaacetic acid (DTPA) as indicated by results obtained in treating six male employees, each of whom has a minute quantity of plutonium within his body. This material had gained access to the body in each case by inhalation due to accidents which occurred at times varying from three hours to eight years prior to the present treatment. With the exception of the one case of recent origin, all cases had been carefully followed for years with frequent analyses of the 24-hour urinary output of plutonium. The effectiveness of DTPA was judged by comparing the average daily urinary output of plutonium after treatment with the average daily output before treatment. Effectiveness in this respect was compared with that of calcium-disodium ethylenediaminetetraaceticacid (EDTA) when possible.

Dr. Norwood is Manager, Health Operation, Hanford Atomic Products Operation, operated by the General Electric Company for the United States Atomic Energy Commission. The DTPA for this study was kindly supplied by Dr. Murray Weiner, Geigy Pharmaceuticals, P. O. Box 430, Yonkers, N. Y. Collection of samples of urine and feces were coordinated by R. H. Wilson. G. D. Brown and staff performed the many bioassays of these samples.

Received for publication September 14, 1959.

In measuring effectiveness of treatment of the acute case, Employee No. 6, the total elimination of Pu^{239} was to be compared with the estimated total body deposition and with the deposition expected if treatment had not been given. Unfortunately, the very small deposition was relatively insoluble and deeply deposited in a healed flesh wound. We shall be unable to estimate the actual deposition for many months and so cannot now determine the effectiveness of DTPA in this case. This case serves to illustrate the fact that, even with the most sensitive whole-body counter and bioassay facilities, accurate estimation of less-than-permissible body burden of poorly soluble plutonium may be impossible for a long time. Only one of the employees (No. 1, Table II) had received a plutonium deposition in excess of the maximum permissible deposit (0.6 μg—0.04μc). This person and Employee No. 2 were previously treated with calcium-disodium ethylenediaminetetraacetic acid, which has been the treatment of choice up to this time.[2, 3] This allowed a comparison of the effectiveness of the two agents as shown in Table I.

Effectiveness of DTPA in Rats

As various chelating agents were developed and studied by a number of workers, it was predicted that several might be more effective than EDTA in averting storage of plutonium in the tissues and in the enhancement of the rate of urinary excretion of metal already deposited in tissues. One of the more promising agents, DTPA, forms a chelate with plutonium which has a higher stability constant than that of EDTA with plutonium. Smith,[4a] at this project, first reported DTPA to be considerably superior to any agent previously used in removing plutonium from rats in both the acute and the chronic stages. Schubert and associates[5] in working with DTPA and

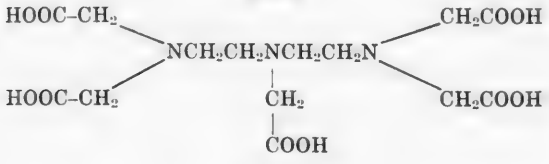
2,2′-bis[di(carboxymethyl)amino] diethylether (BAETA) found both much more effective than EDTA or zirconium citrate in increasing the rate of urinary elimination of deposited plutonium from the bodies of rats. Both groups found that DTPA was effective to great degree even when treatment was instituted weeks after the deposition of Pu^{239} had occurred. Smith[4b] reported that a dose of 75 mg/kg of trisodium-calcium DTPA reduced skeletal deposition of Pu^{239} to less than 20% of that of the controls and liver deposition to less than 10% of the control rats. He also reported that DTPA, alone, is much more effective than when used in conjunction with zirconium citrate in rats. We have not used BAETA in treating humans who have depositions of Pu^{239} but feel that its effectiveness should be determined.

Table I—Effect of DTPA upon Urinary Excretion of Plutonium

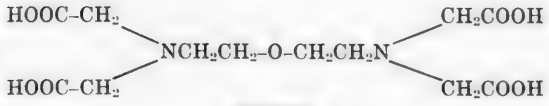
Employee No.	Employee Age	Time prior to treatment at which accidental inhalation occurred	I.V. Dosage of Trisodium-Calcium DTPA (1) Gm/Dose (2) Doses/Day (3) Days of Treatment/Week	Average 24-Hour Urinary Output of Pu^{239} Expressed as Disintegrations per Minute (D/M) Before Treatment	Average 24-Hour Urinary Output of Pu^{239} Expressed as Disintegrations per Minute (D/M) After Treatment	Ratio Pu^{239} Output After Treatment / Before Treatment	Comment
1	43	2.5	(1) 0.1 gm to 0.4 gm (2) Twice daily (3) 5 days/week	7.25	742	102	When treated with EDTA following accident, output of Pu was increased by factor of 10. After cessation of treatment with DTPA, Pu excretion rate was only slowly reduced reaching normal rate only after 2 weeks
			(1) 0.4 gm (2) Twice daily (3) Treat. Mon., Wed., Fri.	7.25	481	67	
			(1) 0.5 gm (2) Twice daily (3) Treat. Mon., Wed., Fri.	7.25	495	68	
2	42	2.5	(1) 0.1, 0.15, 0.2, 0.2, 0.2 gm (2) Twice daily (3) 5 days/week	2.07	102	49	When treated with EDTA following accident, output of Pu was increased by factor of 6. Feces D/M before treatment—1.8; after treatment—12.2
3	35	4	(1) 0.8 gm (2) Once daily (3) Mon., Wed., Fri.	0.12	9.1	76	No appreciable difference in results when single daily dose is compared with 2 daily doses. In this case, the 1.6 gm dose was no more effective than the 0.8 gm daily dose. Feces before treatment—0.58 D/M; after treatment by Dr. Brockman—4.4 D/M
			(1) 0.4 gm (2) Twice daily (3) 5 days/week	0.12	10.3	86	
			(1) 1.6 gm (2) Once daily (3) 5 days/week	0.12	8.7	72	
			1.6 gm once daily, twice a week	0.12	5.0	42	
4	36	7	(1) 0.2 gm (2) Once daily (3) Received only one dose	0.44	20 (Single Sample)	45	Very tense during treatment. On evening following treatment, developed migraine headache and vomiting. Treatments stopped as felt they were too emotionally upsetting. Recovered quickly. Feces before treatment—0.9; after treatment—2.0
5	37	8	(1) 0.4, 0.8, 1.2, 1.2, 1.2 gm (2) Once daily (3) 5 days/week	0.15	18	120	Larger dose no more effective. Feces before treatment—0.55; after treatment—4.7
			(1) 1.2, 1.4, 1.6, 1.8, 2.0 gm (2) Once daily (3) 5 days/week	0.15	14	93	
6	45	3	(1) 1.0 gm (2) Once daily (3) 4 days first week; Mon., Wed., Fri. second week. No further treatment.	0	Inconclusive owing to irregular absorption from deep laceration and lungs		After treatment: BUN, 13 mg/100 cc PSP—Normal 70% dye excreted—1 hour Watery bowel movements during period of treatment. (Given by K. G. Brockman, M.D.)

The formulas of the chelating agents referred to above are shown below.

EDTA



DTPA



BAETA

Toxicity of DTPA in Rats

Schubert's[5b] preliminary acute toxicity studies indicated that at dose levels of calcium DTPA of 1,830 mg/kg no harmful effects were apparent in female rats. This suggested a toxicity for rats only slightly higher on a molar basis than that of EDTA. Foreman's[6] preliminary studies on the toxicity of calcium DTPA in rats indicated that the LD_{50} was about equal to that of EDTA. Even at dose levels as low as 30 mg/kg, however, there was histological evidence of alteration of renal tubule cells. The difference in findings by these two workers indicates a need for further research, and this is in progress. Foreman found that a dose of 75 mg/kg given twice daily was very effective in removing plutonium from the bodies of rats but suspected that a lower dose might have been effective.

Toxicity Experience with EDTA

EDTA is now considered to be less innocuous than it was formerly thought to be. Foreman[7] and associates reported the occurrence of toxic nephrosis in a woman treated with EDTA. Their experiments with rats showed that histological tubular damage occurred in half the animals tested at a daily dose of 203 mg/kg of body weight per day. A number of deaths in humans, due to acute renal failure, have apparently been precipitated by EDTA treatment of persons with renal disease. Brugsch[8] has collected these cases and points out that the fatalities have occurred largely in two groups: (1) those being treated with calcium-disodium EDTA for lead poisoning, and (2) those being treated with sodium EDTA for hypercalcemia. He states: "One must therefore conclude from the data available, that renal disease, if present in patients with lead poisoning will show a particular susceptibility to edathamil. This review suggests strongly that both lead and calcium could act as a tubular damaging substance. Versenate should be given only with proper evaluation of the patient's renal status before, during, and after therapy."

Since preliminary animal studies suggest that the toxicity of DTPA is similar to that of EDTA, even greater caution should be used in treating humans with DTPA until more is known about it.

Effectiveness of DTPA in Humans

We explained to six employees the state of our knowledge concerning DTPA, and they elected to receive treatment to determine its effectiveness in increasing the elimination of the small amounts of plutonium which had been retained in their bodies for variable periods of time. Careful physical examinations were given before treatment was started, and urine was examined before each treatment. The material in 250 cc of isotonic saline solution was administered intravenously by slow drip once or twice a day using a No. 22 needle. As indicated in Table I, the initial dose, 0.1 gm of trisodium-calcium DTPA, was gradually increased to 1.0 gm daily. The result of two weeks of treatment of employee No. 1 is graphically shown in Fig. 1 The daily rate of excretion of Pu^{239} in the urine was increased during this period of treatment by a factor of 68 and was sustained for many days following cessation of treatment. The treatment schedule was 1.0 gm three times a week. A maximum daily dose of 2 gm was given. One employee (No. 4, Table I) was emotionally upset by the experience so was given only the initial dose of 0.2 gm. This millwright, 36 years of age, had received about 0.4 μgm of Pu^{239} by inhalation seven years prior to this treatment. This is two-thirds of the maximum permissible deposition. Numerous examinations of the 24-hour specimens of urine indicated an average of 0.44 disintegration per minute (D/M) prior to treatment. The urinary output of Pu^{239} for the first 24 hours following this single treatment was 20 D/M, or an increase by a factor of 45. Although no further treatment were given, succeeding daily urinary outputs were as follows: day 2, lost; day 3, 17 D/M; day 4, 13; day 5, 8; day 6, 15; day 7, 13; day 8, 8; day 9, 6; day 10, 6; day 11, 8; and day 12, 8 D/M. Sampling was discontinued at this point, but it may be seen that 12 days following a single small dose of DTPA

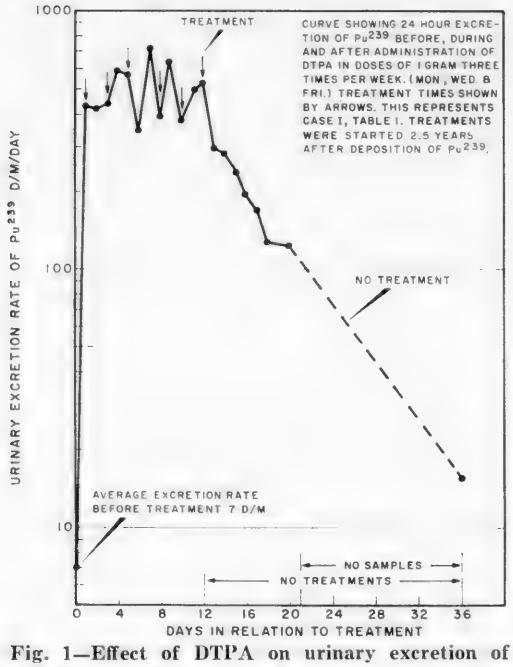

1000
100
10
TREATMENT
CURVE SHOWING 24 HOUR EXCRETION OF Pu239 BEFORE, DURING AND AFTER ADMINISTRATION OF DTPA IN DOSES OF 1 GRAM THREE TIMES PER WEEK. (MON., WED. & FRI.) TREATMENT TIMES SHOWN BY ARROWS. THIS REPRESENTS CASE I, TABLE I. TREATMENTS WERE STARTED 2.5 YEARS AFTER DEPOSITION OF Pu239.
NO TREATMENT
AVERAGE EXCRETION RATE BEFORE TREATMENT 7 D/M
NO SAMPLES
NO TREATMENTS
URINARY EXCRETION RATE OF Pu239 D/M/DAY
0 4 8 12 16 20 24 28 32 36
DAYS IN RELATION TO TREATMENT

Fig. 1—Effect of DTPA on urinary excretion of plutonium from body.

the daily urinary excretion rate of Pu^{239} was still increased by a factor of 20. This sustained action was shown in all cases and suggests that since DTPA is active for so many days following injection at least an appreciable portion is probably retained for many days in the human body. This is in contrast to EDTA in which 95% to 98% of the injected dose in rats is excreted in hours.[9, 10] This significant sustained activity was not found when rats were treated with EDTA.[4, 5]

DTPA Dose Schedule

In trying to arrive at the optimum safe dose, the effect on urinary excretion of Pu^{239} of varying amounts and time intervals was observed and recorded in Table I. We were anxious to obtain data as quickly as possible for use in case of an emergency but wished to be extremely cautious in the use of this new drug in treating employee's deposits which are presumed to be of no clinical significance. Hence, the doses are smaller in number and size than would be the case in a well-controlled series. Dr. A. D. Wiggins, statistician at this project, performed a statistical analysis to assist in drawing conclusions from results shown in Table I.

The urinary excretion data from Employees 1, 2, 3, and 5 were subjected to logarithmic transformation in order to stabilize the within-cell variances, the cells being as in Table II. The transformed data were then analyzed with use

Table II—Number of Observations upon Each of Four Treatment Schedules

Employee	Treatment Schedule Number 1	2	3	4
1	5	38	0	0
2	12	8	0	0
3	4	13	0	5
5	2	0	11	0

of standard analysis of variance techniques. The analysis was conducted under the assumption that the data resulted from a two-factor experiment with each factor occurring at four levels, one of the factors being the effects due to individuals treated and the other being the effects due to differing treatment schedules. Owing to the spotty character of the data, an unbalanced incomplete randomized block design was assumed. The number of observations in each of the cells is given in Table II.

Treatment Schedule 1 consisted of no treatment whatsoever; Treatment Schedule 2 consisted of average administrations of 0.39, 0.28, and 0.40 gm of DTPA per day to Employees 1, 2, and 3, respectively; Employee 5 was the only one appearing at treatment Schedule 3, which consisted of an average administration of 0.9 gm of DTPA per day; Employee 3 was the only one appearing at Schedule 4, which consisted of a daily average administration of 1.6 gm of DTPA.

Of primary interest was the question of whether or not there is a significant difference between the effects due to Treatment Schedules 3 and 4. The analysis indicates that there was no significant difference between daily dose schedules of 0.9 gm and 1.6 gm of DTPA.

More detailed information, on the analysis of the data, is available upon request.

The increased removal of Pu^{239} due to a 1.0 gm daily dose over that due to 1.0 gm administered on alternate days or even every third day was statistically significant, but the advantage was not great enough to warrant use of the medication daily except for a few days immediately following a serious deposition. These conclusions are, of course, tentative. Doses larger than 2.0 gm daily were not given as it was felt unwise to do so until more is known of this drug or until an urgent situation arises. Actually, the analysis of the limited data indicated that not much was to be gained by going to doses larger than 1.0 gm per day.

Employee No. 1, Table I, does have a deposit equaling several maximum permissible limits. His natural rate of elimination had dropped to a low level during the 30 months following his exposure. When he is given 1.0 gm of DTPA

twice a week for three weeks and then no treatment for three weeks, however, the output of Pu^{239} is increased by a factor of about 40. This would result in clearing the body of a permissible limit (0.6 μg) in less than six months; so we plan to continue treatment of this employee on an intermittent basis, checking urines before each treatment and doing kidney and liver function tests at appropriate intervals.

Elimination of Pu^{239} in Feces

In the four employees in which the daily fecal elimination of Pu^{239} was checked before and during treatment with DTPA, there was an increase in the rate by the factors 2, 8, 8, and 7, with an average factor of 6. Larger numbers of tests will be needed since fecal elimination varies greatly from day to day. Since in these few tests the daily fecal elimination before treatment was several times that of the daily urinary elimination of Pu^{239}, even a sixfold increase may prove to be of considerable significance in the total elimination, if a more complete study verifies this early data which is not at variance with the rat studies here.[4]

Increase in Urinary Output of Pu^{239} due to DTPA

As indicated in Table I, increases in the daily elimination of Pu^{239} due to the various doses and schedules of treatment varied from 45 to 120 in employees treated 2.5 to 8 years after the initial deposition. This compares with a multiplication factor of 6 to 10 in two of these employees when treated shortly after the deposition with EDTA. Using this comparison, DTPA would appear to be about 8 to 12 times as effective as EDTA in eliminating Pu^{239} from the human body.

Toxic Effects of DTPA in Man

The largest number of days of treatment for any individual was 18 for a total dose of 14 gm (Employee No. 1, Table I). This was given over a three-month period, and at the end of this series the urine showed no abnormality on routine examination, and good concentrating ability was indicated by large variation in the specific gravity of the numerous samples collected at varying hours of the day. Findings on liver function, kidney function, and blood chemistry tests were as follows: cephalin flocculation at 24 hours, 1+, at 48 hours, 2+; thymol turbidity, 2 units; urobolinogen, positive in dilution 1:20, negative in dilution 1:30; calcium, 10 mg/100 cc; phosphorus, 2.8 mg/100 cc; blood urea nitrogen, 14 mg/100 cc; total protein, 6.9 gm %; albumin, 4.7 gm %; globulin, 2.2 gm %; A-G ratio, 2.1 (Bromsulfalein sulfobromophthalien sodium); test, 2% retained at 45 minutes. All tests are normal with the possible exception of the cephalin flocculation. Our pathologist considered this to be within normal limits. After the fifth day of treatment, in which daily doses were 0.2 gm, 0.4 gm, 0.6 gm, 0.8 gm, and 0.8 gm, the centrifuged urine specimen contained an average of 30 red blood cells per high-power field. Treatment was stopped and the urine on the next and succeeding days showed no abnormality. Eight weeks later, treatment was resumed at a dose of 0.8 gm two or three times a week for five weeks. There were no further abnormalities in the urine analyses.

There were no other abnormal signs or symptoms in the other five employees except in the case noted where nervous excitement induced by treatment apparently led to an attack of migraine, to which the employee was subject. No further treatments were administered to this employee (No. 4, Table I).

Value of DTPA in Treatment for Internally Deposited Fission Products

By analogy with EDTA, we might expect DTPA to be effective in increasing the urinary rate of elimination of mixed fission products and of uranium. It was not expected that DTPA would be of value in increasing the normal rate of elimination of strontium-85, and this is true at least in rats.[5] Kroll and his associates have found that yttrium and lanthanum when chelated with either DTPA or cyclohexane 1,2-transdiaminetetraacetic acid (CDTA) and injected in tracer amounts in humans are eliminated much more effectively than when EDTA is used as the chelating agent.[11] DTPA was proved to be superior to CDTA in this respect. Fried and others[5b] found DTPA much superior to EDTA in eliminating thorium in rats. Catsch and others[12, 13] found DTPA and BAETA more effective than EDTA for removing internally deposited radiocerium from rats. We are not aware of DTPA having been used in the treatment of humans suffering from lead poisoning. Hammond's preliminary screening tests showed DTPA to be only slightly superior to EDTA, at best, in increasing urinary lead excretion in experimental calves.[14] This is not surprising, since the stability constants for these two agents with lead are approximately equal.

Comment

Animal tests have shown DTPA to be the most effective agent discovered to date for removal of internally deposited plutonium.[4, 5] Preliminary animal tests suggest that it is about as toxic to the kidney as is EDTA, which

is presently being extensively used.[5, 6] Treatment of five employees having small internal deposits of plutonium has indicated that the rate of its elimination via the urine is increased by a factor ranging from 45 to 120 when treatment is given 2.5 to 8 years after deposition. Two of the employees had previously been treated with EDTA. When treated with DTPA, the increased urinary output of Pu^{239} was 8 to 12 times that obtained with EDTA.

One employee (No. 6, Table I) was treated three hours following accidental deposition of a very small quantity of Pu^{239}, but irregular absorption has prevented accurate analysis of this case to date. While less impressive, an increase in the fecal rate of elimination was also found. Used in the small doses, which are apparently required, there was no evidence of toxicity with one possible exception. As described, Employee No. 1 showed some red cells in one urine specimen after the fifth day of treatment. This cleared by the following day and remained clear when treatment was later resumed.

Based upon analogy with EDTA, and comparative studies which have been made, it is probable that DTPA will also prove to be the most effective agent[11, 12, 13] for removal of mixed fission products, uranium, and thorium. Tests by others have proved DTPA to be more effective than EDTA in eliminating deposited radioyttrium, lanthanum, and cerium from the body via the urine. It has not proved[5] to be effective in increasing the elimination rate of strontium-85.

Conclusion

DTPA has been shown to be about as effective in treating a small series of humans as previous work by others has shown it to be in removing deposited plutonium from rats. Six humans were treated with doses varying from 0.1 to 2.0 gm of DTPA daily.

Rate of elimination of Pu^{239} via the urine was increased by factors ranging from 45 to 120, which is much better than any agent previously used. One employee developed a mild kidney irritation, possibly as a result of treatment. This cleared over night and did not recur upon resumption of treatment. Treatment should be started as quickly as possible following an accident in which it is estimated that the maximum permissible deposition of Pu^{239} has been exceeded. Where the deposition exceeds the maximum permissible by a large factor, the daily dosage may be doubled or tripled initially. When used for more than a few days, a dose of 1.0 gm two or three times per week for three weeks is recommended to be alternated with periods of three weeks of no treatment. This drug should not be used in the presence of nephritis or other kidney pathology and should be used only with proper evaluation of the patient's renal status before, during, and after therapy.

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Differentiation of Venous Thrombosis of the Lower Extremities

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THE FAIRLY general practice of placing all types of venous thrombosis in the lower extremities into a single category of thrombophlebitis, without attempting further differentiation, is without physiologic, pathologic, or clinical basis. Furthermore, such an approach may cause the physician to lose sight of the possibility of serious complications associated with several of the disorders and hence may result in the initiation of an improper and ineffective program of treatment. Conversely, it may be responsible for the institution of an unnecessary and prolonged period of complete bed rest and for the administration of potentially dangerous medications as therapy for a relatively benign condition.

The purpose of this paper is to present a differential diagnosis of thrombosis of the superficial and deep veins of the lower extremities and to discuss the sequelae which may follow involvement of a main deep venous channel.

Thrombosis of Superficial Veins

Thrombosis of either the great or the small saphenous system is a relatively frequent occurrence. Clinically, two types exist, the commoner entity being superficial benign thrombophlebitis, in which a superficial vein, alone or in conjunction with some of its tributaries, is a site of a thrombotic process. The other, rather rare, condition is thrombophlebitis migrans, typified by occlusion of small segments of superficial veins in one or more extremities. Because of the purely local reaction, superficial thrombophlebitis of either type does not produce any systemic responses. Furthermore, there is no edema of the involved extremity because the pathologic process does not affect the main venous channels involved in removal of blood from the limb.

Superficial Benign Thrombophlebitis—The typical finding in superficial benign thrombophlebitis is a linear area of redness in the skin of the extremity, generally about 1 cm wide and of varying lengths, located in the vicinity of a superficial vein (Fig. 1). Palpation over the involved site discloses an increase in cutaneous temperature and a tender cord-like mass in the subcutaneous tissue. Pain is ordinarily not present unless the involved structure is stretched on movement of the limb.

Fig. 1—Extensive benign thrombophlebitis of superficial veins on posterior surface of left thigh and leg. (From D. I. Abramson: Diagnosis and Treatment of Peripheral Vascular Disorders, New York, Paul B. Hoeber, Inc. 1956.)

From the Department of Physical Medicine and Rehabilitation, University of Illinois College of Medicine.

This paper was presented at the Forty-Third Annual Meeting of the Industrial Medical Association, Chicago, April 30, 1959.

Fig. 2—Thrombophlebitis migrans, with involvement of many segments of superficial veins on both lower extremities. (From D. I. Abramson: Diagnosis and Treatment of Peripheral Vascular Disorders, New York, Paul B. Hoeber, Inc. 1956.)

With recession of the process, the signs of inflammation disappear, to be replaced in most instances by an outlining linear area of brown pigmentation. The vein, itself, however, may remain as a palpable mass for many weeks afterward or, in some instances, even permanently.

Thrombophlebitis Migrans—In the case of thrombophlebitis migrans (idiopathic, recurrent, superficial migratory thrombophlebitis), the changes in the vessel are also inflammatory, but the portions of vein involved are much shorter in length than those observed in superficial benign thrombophlebitis. Clinically, this condition is characterized by the presence of small, red, discrete and tender nodules located on the extremities in the vicinity of superficial veins (Fig. 2). The affected portion of the vessel can be felt as a firm, indurated cord, associated with considerable local rubor. Of importance in differential diagnosis is the finding that the process appears in the form of crops, involving segments of a single vein or of different veins in various portions of the extremities. While some of the lesions are forming, others in the vicinity, or even in the same vessel, show signs of regression. The fleeting character of the nodules is responsible for the name given to this disease. It resembles superficial migratory thrombophlebitis associated with thromboangiitis obliterans, except that in the latter, invariably there is also involvement of the arterial tree some time in the course of the disease.

As the process recedes, the cord-like mass observed in thrombophlebitis migrans becomes less obvious and may then disappear. However, there may be a deposit of pigment to mark the site of the lesion.

Thrombosis of Deep Veins

Whereas thrombosis of superficial veins of the lower extremities in most instances is unassociated with serious complications or sequelae, a similar process in the deep veins may have much graver implications. Because of its close association with pulmonary embolism, deep venous thrombosis may alter the prognosis of a relatively benign illness or surgical procedure. Even when such a complication does not occur, this condition may markedly prolong the postoperative course and convalescent period. In many cases it may also be responsible for disabling sequelae which restrict the physical activity of the patient for months and even years.

An attempt has been made to divide acute thrombosis of the deep veins of the lower extremities into two types: phlebothrombosis and deep thrombophlebitis (phlegmasia alba dolens, milk-leg). Although such a classification has not met with universal acceptance, still there is much in its favor, especially since the clinical picture and the treatment may be different in each disorder. Nevertheless, it is necessary to point out that two entities may represent different phases of the same disease and, furthermore, that histologic examination reveals no changes that differentiate them. On the other hand, either one frequently exists without the clinical appearance of the other.

Phlebothrombosis—In phlebothrombosis there is considered to be a partial or complete occlusion by a bland thrombus of the small deep venous plexuses of the calf or sole. The clot may propagate without becoming particularly adherent to the wall of the vessel; it remains jelly-like in consistency and friable and hence is a frequent source of pulmonary emboli (Fig. 3).

Generally the systemic responses associated with phlebothrombosis are of a minor degree and usually are overlooked. Among these is a slight and simultaneous increase in temperature and in pulse and respiratory rates, for which there is no obvious reason, in an individual who has been at complete bed rest for some time or is convalescing from an operative

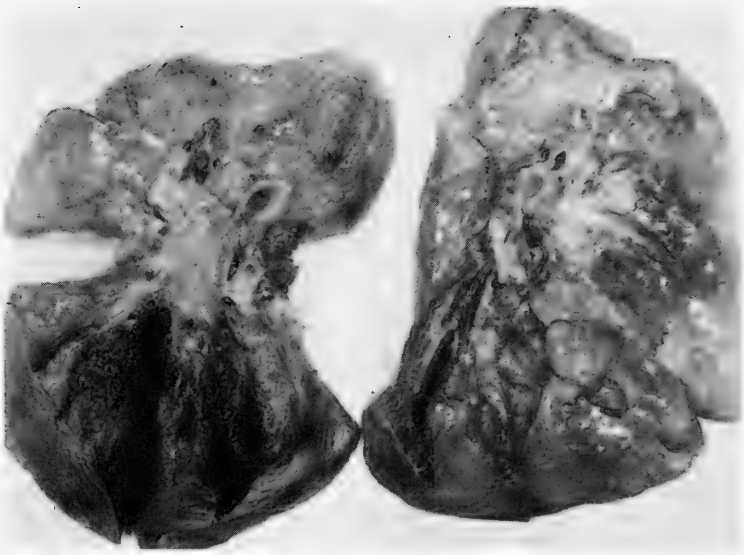


Fig. 3—Extensive infarction in both lungs following massive pulmonary embolism. (From D. I. Abramson: Diagnosis and Treatment of Peripheral Vascular Disorders, New York, Paul B. Hoeber, Inc. 1956.)

procedure. There may also be some apprehension, restlessness, and a feeling of impending disaster.

Since the venous channels involved are small, at least initially, and of little importance in removal of blood from the extremity, there are no clinical signs of local venous stasis. Among the meager physical findings are pain in the calf elicited by dorsiflexion of the foot (positive Homans' sign), tense or spastic calf muscles, an indefinite mass between the bellies of the gastrocnemius muscle, and pain in the lower portion of the leg on passive extension of the foot and plantar flexion of the toes. There may also be a slight increase in the circumference of the calf which is determined only by measurement, for obvious edema is generally not present in phlebothrombosis. Among the localizing complaints is an aching or cramp-like pain in the calf at rest, with tenderness in this site and also in the foot.

Deep Thrombophlebitis—In deep thrombophlebitis the thrombus is located in either the popliteal or the iliofemoral vein and is firmly adherent to the vessel, owing to the resulting inflammatory reaction in the intima. Associated with such changes are a local periphlebitis, involvement of the neighboring lymphatic channels in the process, and reflex vasospasm of the arteries in the limb. Because of the type of response in the lumen of the vein, the tendency for the liberation of emboli is not as great as in the case of phlebothrombosis. However, if there is propagation of the clot beyond the site of origin, the unattached tail of the thrombus may easily be liberated into the blood stream. Since the main venous channels in the limb, as well as the collateral vessels, are generally occluded by the thrombus, marked interference with venous outflow usually occurs, followed by venous stasis, and, as a consequence, a clinical picture which offers no real diagnostic problem.

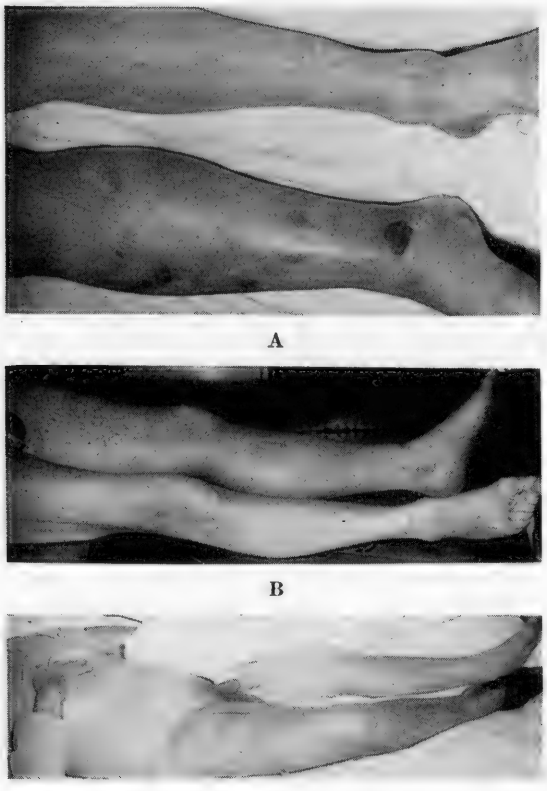
In contrast to phlebothrombosis, constitutional responses are quite prominent in acute deep thrombophlebitis. Among these are fever (temperature up to 102° F), tachycardia, mild malaise, leukocytosis, and a high sedimentation rate.

Among the complaints first noted in the acute stage of deep thrombophlebitis is pain in the involved limb, located either along the course of the affected vessel and in the groin or in the whole extremity. At times the symptom may be very severe. Tenderness is generally present in Scarpa's triangle and in the groin.

The most prominent physical finding is swelling, which appears soon after the onset of the pain, although at times it may occur before any symptom is experienced. Depending upon the degree of impairment of local venous return, the amount of swelling may vary from a barely noticeable pretibial pitting edema to massive involvement of the entire limb (Fig. 4). The leg may appear cyanotic at first, but it rapidly becomes white, owing to compression and collapse of the minute cutaneous vessels by the edema fluid. As the acute stage of deep thrombophlebitis subsides, the swelling becomes less and finally disappears.

Postphlebitic Syndrome

By the term "chronic venous stasis" is meant a persistent state of pooling of blood in, and an overdistention of, the superficial veins of the lower extremities. If this situation exists for more than four or five years, certain changes will result locally, such as the formation of dilated and varicose veins, edema, signs of hypertonus of the sympathetic nervous system, stasis dermatitis, recurrent, chronic indurated cellulitis, and ulceration. These alterations have collectively been called the postphlebitic syndrome. It is necessary to emphasize that the appearance of such changes does not indicate a recurrence of the acute process in the deep veins, but rather that the available venous



A

B

C

Fig. 4—Acute iliofemoral thrombophlebitis. A and B. Marked swelling of involved extremities. C. Massive involvement of deep venous system, with resulting bullae and gangrene of foot (phlegmasia cerulea dolens). (From D. I. Abramson: Diagnosis and Treatment of Peripheral Vascular Disorders, New York, Paul B. Hoeber, Inc. 1956.)

channels are not adequate for the normal venous return from the involved lower extremity. Furthermore, in a high percentage of cases such a state can be prevented by the institution of a proper therapeutic regimen during the acute stage of deep thrombophlebitis.

Dilated and Varicose Veins—A frequent sequel of acute deep thrombophlebitis is the appearance of dilated and varicose veins involving both the great and the small saphenous system (Fig. 5). The alterations are generally due to regurgitation of blood and an increase in venous pressure in the deep venous channels, with transmission of the change in pressure to the superficial vessels through communicating veins. Generally the etiologic factor is recanalization of the thrombosed segment of vessel, with resulting destruction of the valves locally. Less often the increase of venous pressure in superficial veins is due to a shunting of blood into them because of persistence of occlusion of the deep venous channels.

Edema—Another finding commonly observed in the postphlebitic syndrome is pitting edema of the involved limb (Fig. 6). If this change persists uncontrolled over a long period of time, it may be replaced by a brawny, nonpitting lymphedema and the formation of a fibrous reaction which binds all the superficial tissues down (Fig. 7A).

The cause of the pitting edema is an increase in venous pressure, as a result of interference with venous outflow. This is transmitted back into the venules and capillaries and acts as a raised filtration pressure. As a result, there is a greater than normal movement of fluid through the vessel walls into the tissue spaces, with the production of edema.

Swelling associated with the postphlebitic syndrome may, in part, be due to involvement of the perivenous lymphatics during the original episode of deep thrombophlebitis. Subsequently, perivenous scarring occurs, thus producing variable degrees of obstruction of the main lymphatic channels of the limb and, as a consequence, abnormal lymphatic drainage and lymphedema.

Fig. 5—Postphlebitic syndrome demonstrating secondary varicosities of right leg, following iliofemoral thrombophlebitis. (From D. I. Abramson: Diagnosis and Treatment of Peripheral Vascular Disorders, New York, Paul B. Hoeber, Inc. 1956.)

Fig. 6—Postphlebitic syndrome demonstrating chronic edema of left leg, following iliofemoral thrombophlebitis. (From D. I. Abramson: Diagnosis and Treatment of Peripheral Vascular Disorders, New York, Paul B. Hoeber, Inc. 1956.)

Excessive Sympathetic Tonus—The postphlebitic extremity may demonstrate signs of increased activity of the sympathetic nervous system, such as cyanosis, reduced cutaneous temperature, and hyperhidrosis. It is possible that these abnormalities result from stimulation of sympathetic nerves through a reflex initiated by the segment of thrombosed vein acting as a focus of irritability. Another etiologic agent may be the long period of physical inactivity to which some patients with deep thrombophlebitis are subjected in the course of treatment.

Pigmentation—Chronic venous stasis is associated with the deposition of brownish pigmentation in the lower third of the leg (Fig. 7B). The basis for this response is not known, although the possibility has been suggested that the change follows deposition of hemosiderin in the tissues. It may also represent capillary hemorrhages due to high venous and capillary pressure, present in venous stasis.

Stasis Dermatitis—A relatively serious sequel of deep thrombophlebitis is stasis dermatitis. It is usually of the weeping eczematous type and is frequently associated with intense itching. The alteration is probably related to the rise in capillary filtration pressure and an associated increase in capillary permeability, permitting the movement of protein-rich fluid through the vessel wall into the tissue spaces.

Stasis Ulceration—The most disabling of the sequelae of acute deep thrombophlebitis is stasis

A B C

Fig. 7—Postphlebitic syndrome. A. Marked fibrotic changes in subcutaneous tissue encircling entire lower portion of leg to produce a tight constricting band. B. Brown pigmentation. C. Extensive stasis ulcer.

ulceration (Fig. 7C). It has definite economic implications, since, once it has developed, it frequently renders the patient a semi-invalid, incapable of working for weeks or months. Furthermore, it has a definite tendency to recur.

The cause of the stasis ulcer is also the increase in venous pressure, with a consequent building up of pressure in the capillaries. The resulting waterlogging, combined with such factors as anoxia, impaired nutrition, and accumulation of toxic waste products of metabolism, reduces the resistance of the skin. As a result, even minor bruises, abrasion, or infections may now produce an ulcer, or the lesion may form spontaneously. The medial and, less often, the lateral aspects of the ankle are the sites of stasis ulcer, primarily because the protective pad in these locations is poor and the possibility of exposure to trauma is great.

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THE RELATIVE POTENTIALS OF

Common Organic Solvents as Precursors of Eye-Irritants in Urban Atmospheres

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RESEARCH of the last few years[1, 2] has demonstrated rather conclusively that eye irritation, as well as other typical effects of urban air pollution of the Los Angeles variety, can be produced by irradiation of synthetic atmospheres containing hydrocarbons and oxides of nitrogen. Investigation has shown that olefins are especially reactive under these conditions, which lead [1, 3, 4] to the production of aldehydes, ozone, organic peroxides, and particulate matter as well as other substances (including the unidentified lacrimators). On the basis of these studies, most of the eye irritation encountered in the Los Angeles Basin is now attributed to the effects of photochemically induced reaction of oxides of nitrogen with the 1,450 tons of hydrocarbons emitted daily into the atmosphere, mainly by motor vehicles.

When a study by members of the Air Pollution Control District staff[5] showed that emissions of organic-solvent vapors approximate 400 tons daily, it was recognized that proper evaluation of the resulting atmospheric pollution depended on knowledge of the potential of these materials for causing the typical "smog symptoms." As the first part of a program for the study of air-pollution effects of solvents, a screening program for eye irritation has been undertaken. This was designed to reveal how the eye irritation potentials of the most common solvents compare with those of the hydrocarbons found in motor-vehicle fuels and exhaust gases. Other aspects of the smog-forming potential of solvent vapors, such as formation of aerosols, production of oxidants, and damage to plants, will be studied separately.

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Measurements of eye irritation potential have been performed with 17 substances widely used as industrial solvents, each at two concentration levels, respectively 20 and 5 ppm (parts per million) by volume, with added nitrogen dioxide at 1 ppm. At the 5 ppm level, measurements have been made with four additional pure hydrocarbons included for reference purposes. Since these measurements concern a physiological response which is subject to considerable individual variation, the data have been subjected to simple, standard statistical procedures to define the real degree of reproducibility of the results and to indicate the extent of agreement between tests run at different concentrations.

Materials

Hydrocarbon Fractions—According to the previously cited survey[5] of organic-solvent usage in Los Angeles County, aliphatic hydrocarbons of various boiling ranges constitute about two-thirds of the total. Since it was obviously impractical to compound samples which would be truly representative of the over-all usage of such materials, tests were done individually on a set of six samples of various boiling ranges. The information furnished by the supplier of these samples is set forth in Table I. (The sample designations are not those used by the supplier.)

Bromine number tests showed no detectable

Table I—Characteristics of Hydrocarbon-Fraction Solvents

	A-1	A-2	A-3	A-4	A-5	A-6
Boiling range,						
lower limit °F	110	142	209	300	310	355
upper limit	264	160	288	400	358	448
	0.6988	0.6902	0.7467	0.7994	0.7981	0.8236

olefin in any of these samples. Mass spectra of the two most volatile samples, A-1 and A-2, were obtained; these showed the presence of aromatics (5% to 10% and 2% to 3%, respectively) and suggested the presence of naphthenes.

Individual Compounds — The remaining materials were represented by samples from laboratory stocks, except for the chloroethylenes. No further purification was attempted, but mass spectra were obtained for each sample and compared with standards, where available, to prevent errors in identification or the accidental use of grossly contaminated material. Compounds studied were 2-propanol (isopropanol, or isopropyl alcohol), ethanol (ethyl alcohol), trichloroethylene), butanone (methyl ethyl ketone), toluene, xylene, propanone (acetone, or dimethyl ketone), methanol (methyl alcohol), hexane, 4-methyl-2-pentanone (methyl isobutyl ketone), tetrachloroethylene (perchloroethylene), 2-ethyl-1-butene, 2-hexene, and 2-methylpentane. These were of the highest purity, except as described below:

1. *Ethanol:* Contained approximately 4 mol per cent water.

2. *Trichloroethylene:* Although no reference scan was available, the mass spectrum showed the absence of appreciable contamination due to compounds containing methyl or methylene groups or compounds of molecular weight higher than that of trichloroethylene. The sample was a commerical degreasing preparation.

3. *Methyl ethyl ketone:* Minor mass peaks at 59 and 60 suggest a small amount of impurity, such as acetic acid. There was no indication of contaminants of molecular weight higher than the ketone.

4. *Toluene:* Small peaks in the range 104 and 106 indicated the probable presence of small quantities of the xylenes. No other impurities were evident.

5. *Xylene:* The sample was a mixture of ortho, meta, and para xylene; its spectrum revealed no unexpected peaks when compared with reference spectra of the individual materials.

6. *Methanol:* A slight impurity was indicated by small peaks for masses 43 and 58. Ethanol was not detected.

7. *Perchloroethylene:* Although no reference scan was available, the mass spectrum showed the absence of any appreciable contamination with hydrogen-containing compound. The sample was a commercial degreasing solvent.

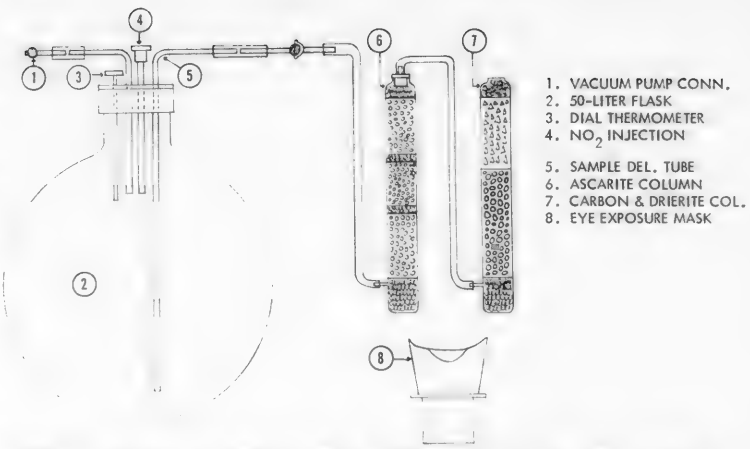

Fig. 1—Diagram of 50-liter flask with ascarite and carbon columns attached. This assembly is used during purging and in bringing flask back to atmospheric pressure after introduction of sample. Ascarite column only is used during sample introduction. Columns are detached during irradiation. Eye exposure mask is inserted directly into mouth of flask.

Experimental Procedure

Apparatus used in the eye-irritation measurements is shown schematically in Fig. 1. A clean, dry 50-liter Pyrex flask, fitted with a stainless-steel adapter, was evacuated to a pressure of about 10 cm Hg. The calculated amount of solvent necessary* to produce the desired concentration was introduced, as a liquid, from a graduated capillary pipet into the stainless-steel tubing of the adapter† and swept into the flask with a small volume of laboratory air. This was followed by a calculated aliquot of a dilute mixture of nitrogen dioxide in air (previously prepared in a 5-liter flask capped with a rubber serum stopper), transferred by means of a syringe and hypodermic needle through a short piece of rubber tubing attached to the stainless-steel adapter. Next, 0.1 ml of water was injected into the system, after which air was admitted to the flask through a tower containing activated carbon and a calcium sulfate drying agent until atmospheric pressure was reached. A 500-ml sample was removed for nitrogen dioxide analysis by the Saltzman procedure,[6] to confirm that the intended concentra-

*For this calculation, each hydrocarbon-fraction sample was arbitrarily assigned molecular weight corresponding to the individual paraffin nearest the center of its boiling range.

†In the first few tests, using 20 ppm of various individual compounds, the liquid was first evaporated in a 5-liter flask, from which aliquots of the gas were removed. This proved inconvenient, especially for the high-boiling hydrocarbons, so the procedure was revised as indicated.

tion was obtained, and then the flask was irradiated.

In the eye-irritation tests which have become standard in this laboratory, the flask was illuminated by four 400-watt mercury vapor lamps situated in a square array around it, within a cubical sheet-metal housing through which the neck of the flask projected, with its stainless-steel adapter. Heat from the lamps caused the temperature of the system to rise to about 110°C (230°F) in an hour of irradiation. (For control tests, opaque shields were inserted between the lamps and the flask so that the mixtures received no actinic radiation.) After an hour, the flask was removed from the irradiation housing and placed in a heating mantle. In about 15 minutes, it cooled to a temperature of 56° to 60°C, which was maintained by adjustment of the power input to the mantle. Another 500 ml sample was removed for determination of the residual concentration of nitrogen dioxide; the adapter used in filling the flask was then removed and an eyepiece adapter substituted. This adapter is designed with a metal shutter to control access of the warm atmosphere to the eyes of exposed panelists and minimize the loss of the test atmosphere by convection in the intervals between exposures.

In the tests with solar irradiation, the procedure was the same, except that no housing was used, the flask being placed in direct sunshine. The temperature was raised only slightly by this exposure; typical resulting temperatures after one hour in the sun were 30° to 40°C; hence it was necessary to heat the flask before making the panel exposure at 60°C. This was accomplished by the heating mantle mentioned above.

For the determination of a numerical eye-irritation index, a panel of 8 to 11 persons was chosen more or less at random from the staff (although some individuals participated much more consistently than others). Each in turn exposed his eyes to the warm irradiated atmosphere and reported when he detected irritation. The time in seconds was recorded, unless it was more than 90 seconds, in which case the exposure was terminated and the value recorded as 90. For statistical evaluation, the eye-irritation index is taken as $100 \log 100/t$, where t is the average response time. This defines an index which approaches the value 100 as the panel response time approaches 10 seconds, which may be considered to represent very strong eye irritation; the minimum possible index value in the experiments reported here was 5, corresponding to an average response time of 89 seconds or more. Other studies in this laboratory have shown that, with standard irritants, this index is approximately a straight-line function of the logarithm of the irritant concentration.

Results and Discussion

Table II presents, in successive columns, the eye-irritation indices for standard tests run at the 20 ppm level and the 5 ppm level, control tests in which there was no exposure to light, and solar-irradiation tests. Constant experimental conditions throughout the tests were 1 ppm initial concentration of nitrogen dioxide and one hour allotted reaction time. The figures entered in the table represent the averages of two panel determinations or in a few cases more, as indicated. Based on the replicate determinations as well as other experience with the same method in this laboratory, the standard deviation of individual index values is estimated at 16 units or less through the range of index values here encountered; consequently, the 95% confidence limits for the values cited in the table lie at about 23 units above and below the values cited.

The control tests were run for the five individual compounds which produced the highest values of the eye-irritation index in the initial screening at 20 ppm. In no case did more than half the panel members report eye irritation within 90 seconds of exposure in a control test. The range of values cited for the control tests, viz., 5 to 10, may be considered to represent negligible eye irritation.

In the tests using solar irradiation, eye-irritation indices ranged from 5 to 13 (i.e., negligible or very slight irritation) for all the compounds tested except 2-ethyl-1-butene, the only nonchlorinated olefin on the list. This indicates that, for these irradiated mixtures, the concentration of irritant developed did not exceed the 90-second threshold for most of the subjects. It does not demonstrate that differences in eye-irritation potential would be negligible if exposure periods were lengthened to, say, 5 minutes or 30 minutes. Indeed, the classical theory[7] relating reaction time to irritant concentration implies that, in the general case, such differences will persist at lower concentrations. The results shown in Table II furnish no information on this point, but earlier studies[8] in this laboratory, in which the same method was used to study the eye-irritation potential of irradiated automobile-exhaust gases, indicated that extensive bodies of data on such mixtures are satisfactorily represented by the classical theory. In previous comparisons[9] of the relative effects of irradiation by sunlight and by

Table II—Eye-Irritation Precursor Indices[a] for Commonly Used Solvents and Certain Other Hydrocarbons

Solvent	20 ppm Hg lamps	5 ppm Hg lamps	20 ppm Heat only	5 ppm Sunlight
A-4	30[c]	21		11[b]
A-5	60	14		13
A-6	40	37		11[b]
A-1	29	16		6[b]
A-2	48[c]	31		8[b]
A-3	50[c]	16		13[b]
Isopropanol	12[b]			
Ethanol	20			
Trichloroethylene	56[d]	25	10[b]	7[b]
Methyl ethyl ketone	45	29	9[b]	9[b]
Toluene	32	22		7[b]
Xylene	46	48	6[b]	12[b]
Acetone	9[b]			
Methanol	40	11[b]	8[b]	6[b]
Hexane	29	8[b]		5[b]
Methyl isobutyl ketone	56	63	5[b]	8[b]
Perchloroethylene	7[b]			
2-Ethylbutene-1		47		26
Hexene-2		36		
Cyclohexane		21		6[b]
2-Methylpentane		15		8[b]

a. Eye irritation precursor index = 100 log 100/t, where t is the average response time of the members of a panel of eight to eleven persons. Indices cited are the average of two or more panel determinations. 1 ppm NO_2 was used in all tests.

b. In these tests, fewer than half the subjects detected any eye irritation within the 90-second exposure period.

c. Average of three panels.

d. Average of six panels.

mercury lamps, it has been found that the artificial light yields indices averaging about 30 units higher than the sun, as a result of the combined influence of increased intensity and higher temperature of reaction within the flasks. The data of Table II are consistent with this order of magnitude.

A useful comparison of the results of the screening tests at two different concentration levels is provided by the rankings shown in Table III. For ranking purposes, a single average value has been assigned to represent all the hydrocarbon-fraction solvents listed in Table II. This approach seems justified in view of the evidence that eye-irritation values are not correlated with boiling points for these substances; presumably such differences as exist are determined, rather, by compositional differences among the samples. The additional compounds tested at 5 ppm have been assigned subsidiary ranks to facilitate comparison of the ranks assigned to the solvents themselves.

Comparison of the rankings thus obtained at 20 ppm and at 5 ppm shows that the order of the eight solvents which appear in both is nearly the same in both. The extent of agreement can

Table III—Solvents and Other Compounds Ranked According to Eye-Irritation Potential at Two Concentration Levels

	20 ppm		5 ppm	
	Index	Rank	Index	Rank
Methyl isobutyl ketone	56	1[a]	63	1
Trichloroethylene	56	2[a]	25	4
Xylene	46	3	48	2
Methyl ethyl ketone	45	4	29	3
Hydrocarbon fractions	41	5[a]	23	5
Methanol	41	6[a]	11	7
Toluene	32	7	22	6
Hexane	29	8	8	8
Ethanol	20	9		
Isopropanol	13	10		
Acetone	9	11		
Perchloroethylene	8	12		
2-Ethyl-1-butene			47	2A
2-Hexene			36	2B
Cyclohexane			21	6A
2-Methylpentane			15	6B

a. For pairs of solvents showing the same eye-irritation index, relative ranks were based on the panel medians.

be expressed by Spearman's Rank Correlation Coefficient, which is found to be 0.90.‡ The chance that this agreement would be found by accident, if the rankings were really random rankings, can be tested by Student's method; it is found to be less than 1 in 100. Thus, it is seen that the order of decreasing potency of these solvents was not seriously changed by changing the solvent concentrations used in the tests.

For individual solvents, the significance of the differences between index values at the two levels of concentration is low because of the relatively large standard deviation and the consequent overlapping of the confidence limits. The average effect of the change of concentration from 20 ppm to 5 ppm, nevertheless, can be readily evaluated. It amounts to a decrease of 14 units in the index value and is significantly different from 0 at the 95% level of confidence. The data are inadequate to demonstrate any differences between individual solvents in respect to the dependence of eye irritation on concentration. But, in terms of panel response time, the average effect of the fourfold reduction in solvent-vapor concentration was to increase the response time by about 40%.

The data presented can, of course, be used to compare the individual solvents in pairs; briefly, the eye-irritation potentials of any two of these solvents differ significantly at the 95% level if their indices differ by 32 units or more. Table IV lists the pairs found to differ significantly by this test using the data at 20 ppm.

‡1.0 would indicate complete agreement; —1.0 would indicate complete disagreement; 0.0 would be expected for comparisons of random rankings.

Table IV—Pairs of Solvents for Which Significant Differences in Eye-Irritation Potential Have Been Demonstrated, According to Screening at 20 ppm.

	Ethyl Alcohol	Isopropyl Alcohol	Acetone	Perchloroethylene
Methyl Isobutyl ketone	+	+	+	+
Trichloroethylene	+	+	+	+
Xylene		+	+	+
Methyl ethyl ketone		+	+	+
Hydrocarbon fractions			+	+
Methyl Alcohol			+	+

(+ indicates difference is significant at 95% level; less potent solvents given at top.)

The problem of how to apply the screening data to the estimation of effects of atmospheric contaminants under smog conditions has no single, definitive answer. If it is assumed, however, that the relative order of eye-irritation potential persists down to atmospheric concentrations, several facts suggest that the over-all effect of these solvent vapors in the air may be similar in magnitude to what would be observed if they were replaced by an equivalent amount of gasoline vapor. In the first place, the main bulk of gasoline used as motor fuel also comprises aliphatic hydrocarbons and, although these may differ from the solvent aliphatics in molecular weight and boiling point, their eye-irritation potentials are probably comparable. Secondly, the most reactive solvent species tested (methyl isobutyl ketone and trichloroethylene) seem only about as potent as the most reactive olefins, which are characteristic of most gasolines. Consequently, as a first approximation, it may be warranted to compare solvent emissions with motor-fuel emissions on a ton basis. This leads to a first estimate that the solvent vapors might contribute as much as 25% of the organics in smog. The hydrocarbons emitted in auto exhausts, however, have higher eye-irritation potential[2] than the motor fuels burned because of their enhanced olefinic content. A somewhat more refined estimate, based on linear combination of the eye-irritation indices measured in this laboratory and conversion of the tonnage (or gallonage) figures on emissions to a mol basis, leads to a value of the order of magnitude of 10% for the contribution of solvent vapors to the total eye-irritation potential of the Los Angeles Basin. Thus, it appears that the solvent contributions are small, but probably not negligible, relative to the total.

Summary

The degree of eye irritation produced on irradiating air containing various solvent vapors, each with nitrogen dioxide, has been measured. Of the 12 solvents most used industrially in Los Angeles County, none showed appreciably greater potential for producing eye irritation than did the olefins, 2-hexene and 2-ethyl-1-butene, which were included in the series for purposes of comparison.

At least two-thirds of the solvents tested showed eye-irritation potential at least as great as that of *n*-hexane, which is one of the less active paraffinic constituents of gasolines. Those solvents less active than *n*-hexane are ethanol, isopropanol, acetone, and perchloroethylene.

Among various hydrocarbon-fraction solvents, the eye-irritation potentials do not correlate with the boiling points. Presumably, such differences as exist are determined by compositional differences between the samples.

Screening at 20 ppm and at 5 ppm gives essentially the same order of ranking for the solvents compared; the probability is less than one in a hundred that the observed agreement could have arisen by chance. Thus, the order of decreasing potency of the solvents tested appears to be nearly independent of concentration in these experiments.

The assumption that the relative eye-irritation potentials observed would also apply at atmospheric concentrations leads to an estimate that the potential contribution of solvent vapors to eye irritation in the Los Angeles Basin may be about one-tenth of that due to automobile exhausts and gasoline vapors.

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Discussion by Robert E. Eckardt, Ph.D., M.D.

An alternate conclusion that might be reached from the Wayne and Orcutt studies is that, in the absence of automobile exhaust, solvent vapors in the Los Angeles area would not produce any eye irritation and in the concentrations found in Los Angeles make no significant contribution to the eye irritation problem. It is my contention that to attempt to read more into data than is actually present in data is unjustified and unscientific. I would have no criticism of the Wayne-Orcutt paper if the fifth paragraph were deleted from the Summary and the phrase "in Urban Atmospheres" were deleted from the title. If this were done, then the *data presented* would support the title and conclusions. As it now stands, the *data presented* have no relationship to urban atmospheres, since the concentrations of solvents used and the temperatures of irradiation have no relationship to anything that exists in urban atmospheres. They are strictly experimental conditions designed to obtain positive effects, not to simulate urban atmospheric conditions. Since irradiation of solvent vapors at concentrations far above those found in urban atmospheres, but at temperatures simulating urban temperatures, produced no measurable eye irritants, it is conceivable that no eye irritants were produced at these temperatures. We in the petroleum industry know that cracking of petroleum will proceed at commercially feasible rates when the temperature is elevated to over 1000° F, but may not occur at significantly measurable rates at temperatures under 800° F. Therefore, that reactions occur at 110° C (230° F) which may not occur at all at 30-40° C (86-104° F) should not be surprising.

NATIONAL TUBERCULOSIS ASSOCIATION FELLOWSHIPS

As the Medical Section of the National Tuberculosis Association, the American Thoracic Society (formerly the American Trudeau Society) provides fellowships and traineeships for the graduate education of investigators and teachers in the field of respiratory diseases and tuberculosis. The following types are offered:

Edward Livingston Trudeau Fellowships: A few fellowships at a higher level of training and award are offered to specially qualified candidates with an M.D. degree who have been assured of a continued teaching or research appointment upon completion of training. Trudeau Fellowships are awarded for one year but may be renewed up to a total period of four years.

Research Fellowships: Postdoctoral fellowships are offered to candidates holding the degree of M.D., Ph.D., or Sc.D. for further training as scientific investigators.

Predoctoral fellowships are offered to graduate students with a bachelor's degree to work on a research project for an advanced degree other than M.D.

Teaching Traineeships: Physicians entering their second or third year of residency in Internal Medicine or Thoracic Surgery at a medical center who may be interested in a career of medical teaching are offered traineeships toward that end. Supplementation of these awards by the institution involved is not necessary.

Each applicant for an NTA fellowship or traineeship must have been accepted by the head of the department under whom he expects to work for the next academic year in this country. Awards are determined by individual circumstances and are paid directly to the fellow on a quarterly basis. They are granted for one year, beginning on any date after April first, and are renewable for a total of three years.

All applications must be submitted by November 1st. Further information about fellowships may be obtained upon request from: Director of Medical Education, American Thoracic Society, 1790 Broadway, New York 19, New York.

Retirement—An Orientation and a Method of Industrial Approach

Roger F. Lapham, M.D., White Plains, N. Y.

WEBSTER'S dictionary of synonyms defines "retire" by quoting Shaw: "When he dies or retires a new man must be found." An excellent illustration of our conception of retirement as the end of all activity—a synonym for death.

Industry's present attitude toward retirement compares with medicine's attitude toward psychiatry 25 years ago, when a prominent psychiatrist stated that the medical profession had yet to learn that caning chair seats was insufficient treatment for the mentally ill executive. In arguing whether industry should begin retirement training when the employee is 55 or 60 years old, we forget that we have no realistic program for *any* age, and also that postponing retirement training until 55 makes no more sense than postponing reading lessons until that time.

Intelligent understanding of retirement requires a backward glance to see how it originated and what it is. Today's 55-year-old person will remember to about 1910, when retirement was undreamed of except by a wealthy handful to whom it meant compulsion by illness. In 1910 leisure was nonexistent. Vacations were limited to the rich: summers at the seashore or mountains, where the head of the family spent as little time as possible. And since the "substantial" 1910 businessman belonged to the unlock-the-door-in-the-morning-and-lock-it-at-night school, free time was rarer for him than for his employees.

Laborers and "white collar men" at that time could die in their boots, or remove them and die of starvation; the business owner, 1910's only executive, could die in his boots or remove them and die of boredom. These were the good old days of timeclocks and sweatshops, when retirement was as unknown as pensions and savings plans and one would not have known how to use leisure had one had it.

Life in 1910 divided itself into only two periods—school and work. Today arbitrary limitation of our working years in our 60's, plus lengthening life expectancy, has added to our lives a long third period, retirement. Moreover, pensions and savings plans support us during this period. Economically we are becoming prepared for leisure; emotionally we still use it the way Whistler's mother did.

Thus we see the futility of worrying about beginning retirement training at 55 instead of 60. Retirement is the process of switching from the second to the third period of our lives; more practically, of changing from the activities of work to the activities of leisure. Since emphasis in both periods is on *activity*, preparation for both periods must begin early in life and continue all through it.

During 25 years' medical practice, I have repeatedly asked patients of all ages their plans for retirement. Their answers divide them into two groups: Group I, with no retirement plans ("I'll have plenty of time to think of that when the time comes."), and Group II, a fifth the number of Group I, with so many interests and activities that they are eager to retire. Group I persons never think or look beyond the day's routine, while Group II persons constantly reach beyond their bread and butter.

Since much financial planning has been done for the retiree, let us presently consider only his emotional problems—and it should be emphasized that by meeting the retiree's emotional problems industry will render great service, not only to the employee, but to itself as well. Both these services—financial planning and meeting emotional problems—assumes tremendous importance in a growing social climate of portraying industry as a crushing monster. And the potential of both these services will

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increase with growth of retirement training experience, and growth of population.

Although the age of 65 for retirement has become fairly universal, the figure is certainly open to question. No arbitrary retirement age has any real physiological basis, since some employees are productively finished before 50 and a few Churchillians are highly productive in their 80's. Nevertheless, most persons familiar with the subject feel that until we have greater experience with retirement programs the difficulties of administering a program based on employee's productive capacity (with its constant "Bill Smith is still working, so why can't I?") make it impractical, despite the fact that it is fairer and should be more functional. Some firms compromise by having a 65-year retirement age, with provision for extra years in "special cases," but even here it is doubtful that advantages offset the added administrative difficulties.

The question of area of responsibility for the retirement program is most important: Our legion of retirees with no prospect except vegetation and death points at industry a strong accusation of neglect. But on whom falls the blame—personnel, management, or the industrial physician? Actually, although all three have attractive arguments of rationalization for their neglect, all three share responsibility. Management certainly cannot legitimately say that the welfare of a man who has given a life of service is no longer its concern. Ignoring all humane considerations (and management is proving itself increasingly humane in employee relations other than those with the retiree), good business alone demands a solution of the retiree's emotional problems equal to that of his economic ones.

And if management is responsible it can act only through those trained in employee relations, its personnel, on whom rests responsibility for executing its program.

But perhaps the heaviest responsibility comes finally upon the one trained to recognize and treat nervous and emotional problems—the industrial physician. It is he who must spark a program, and he who must give the support and advice capable of bringing the program to its ultimate potential of drawing in the younger employee, for whom there is real opportunity of creating an active third period of life.

Let us start our consideration of the retirement training program by looking at John Smith, a typical retired man—typical because he had no retirement training and also because each facet of his situation has a counterpart in all retirees so neglected, from the porter to the president. John Smith in his middle 40's was an executive in a retail store. Through his own efforts and those of two associates, his store merged with two others, making him vice-president of a combine which in 20 years grew to a huge retail chain. At 65, by corporate policy, J. S. was retired. Seemingly here was a situation most propitious for successful retirement: He enjoyed excellent health, and financially he could indulge any whim. Yet when I first saw him after retirement, there was not even opportunity to question him before he grabbed my shoulders and in panic poured out the following, quoted practically verbatim:

> Oh heavens, man—my company's policy is just plain murder; they don't leave a man a thing to live for. You must do something to influence corporations to be more humane. There's nothing for me to do but die on the vine, and I'm doing that so fast I even see it myself.

His remarks summarize tragedies which industry is presently turning out at every income and echelon level, hundreds of thousands of times yearly. Consider factor by factor what happened to J. S. (and happens to most of our retirees today), and compare these factors to the same ones in a positive program.

DIRECTION OF THE PROGRAM

J. S., like most retirees, had *no training*—sufficient commentary on its direction. In corporations having retirement training, its direction usually suggests preparation of the retiree for a trip over Niagara Falls in a barrel; a pat-on-the-back, tear-in-the-eye attitude which says, "Well old man, this is something we all face eventually. We can only sympathize, but since we must go through the motions of helping, let's get on with it." (Chair caning.)

Positive Approach—Face the fact that although with oldsters you won't accomplish as much as with youngsters, a constructive program plus a *positive* attitude can give *something*, even if the program begins only six months prior to retirement. But particularly with oldsters, remember the direction of the program is even more important than its specifics. Visualize the retiree as a person facing the same situation you'll soon face, and know that you can help him cultivate the following activities for retirement.

OUTSIDE INTERESTS

J. S.'s greatest deficiency was outside interests. His every thought and activity had always been directed to his work, impinging even upon family relationships to the extent that his daughters grew up almost strangers to him. His business absorbed him to the extent of crowding him away from persons associated with him in it. As a result he had become an increasingly "tough business man"—another way of saying a detached lonely man.

Positive Approach—In surveying 5,000 of its retired employees, the Metropolitan Life Insurance Company found the degree of the employee's success with retirement to vary directly with the number of his outside interests and activities (i.e., interests cultivated before retirement, and not directly related to work). All students of retirement agree with this. So important are outside interests that it can be stated that a retiree with financial security and adequate outside interests will have a successful retirement, regardless of other factors. Outside interests are the most important single factor of the retirement program.

The benefit of outside interests is closely related to the extent to which they bring the retiree into contact with other persons. Thus, civic affairs work is preferable to stamp collecting, while a combination of "personal contact" and "solitary" interests is preferable to either alone. Discussion groups should be held to encourage employees' activity in local civic groups, scout and big brother movements, and to help them with such work, once started. Industry should also encourage employees' cultivation of outside interests through art classes and exhibits of employees' work, music appreciation lectures, garden clubs, glee clubs, and hobby groups and exhibits.

Look, if you will, only at immediate corporate benefits: Other factors being equal, the employee with outside activity will be a better performer than the one without, and will also be a more cooperative member of the group or "team." So in corporate reward alone, such a program pays well—and the resulting benefit to the employee of retirement preparation is a tremendous "extra."

Warning should be given to retirees against using false interest claims to avoid retirement preparation. Two common examples are volunteer work and travel:

Many persons completely unprepared for retirement shrug off their short-sightedness with the statement, "Oh, when I retire I can give some time to my hospital or Red Cross." If the retiree learns and becomes interested in the work prior to retirement, it may prove a successful outlet; but tried as a last resort after retirement it usually proves a depressing experience, as work given for nothing is often valued at just that by all concerned. And not without reason. Volunteers too frequently approach this work as something to do only if they have nothing better; this attitude produces poor work and undependable attendance, giving those in charge visible disrespect for the volunteer and his work.

Travel, like volunteer work, can be a delusion to unprepared retirees. The couple who do not, prior to retirement, travel regularly (part of each vacation) and with an objective (e.g., awareness of the political and social backgrounds of the countries they visit) will see little outside the ship's bar when they finally abruptly begin "traveling" after retirement. In addition to the usual frustrations of unprepared retirees, these people must cope with homesickness. By contrast, travel for prepared retirees offers limitless challenge, and incidentally the more they let themselves see and learn, the less they will need to depend upon the expensive luxury of "first class."

VACATION POLICY

J. S., being an "old school, substantial business man," never had any real vacations, which were to him a mark of weakness. What traveling with his family he could not squirm out of, he combined with business. So never having had experience with leisure before retirement, he is naturally unable to cope with it after retirement.

Positive Approach—Vacations should be put into retirement training by increasing vacation time with age and length of employment. Three weeks' yearly allowance after ten years, and a month after fifteen to twenty years of employment is becoming widespread. In addition, some firms insist that executives over 55 take as much vacation as they wish with a minimum of six weeks yearly. And here insistence is important, for there are always hangers-on of the old school, who will take time off only if forced to do so. Such management policy is neither radical nor costly, for the conscientious executive won't abuse it, while the executive who will is low-productive and his excessive vacation is no real corporate loss. To the corporation such policy presents several advantages: The man rested and broadened by change of scene works better than the tired, stale employee, and progresses faster and further. Nor is this increased progress limited to the one employee. The younger executive is better prepared to sit permanently at his supervisor's desk, when the time comes, by the opportunity to shoulder his superior's responsibilities during the latter's increasing vacation absences. The jealous and uninterrupted guarding of a job by one man until his sudden relegation to the ash-heap by retirement can be disastrous for the man, for his successor, and for the job itself.

Accompanying progressive vacation policy, publicity should be given these vacations as small trial retirements, as opportunities for trying out activities and finding interests for permanent retirement.

RETIREMENT LITERATURE

J. S. never saw any retirement literature

and if he had he would have blasphemed it (not without some reason) as a lot of hogwash. Much literature directed at the retiree today has a strong Pollyanna tint, being hopelessly over-simplified and idealized—the rose-covered cottage treatment, which merely hints at or ignores completely practical problems and emotional factors.

Positive Approach—One of the more practical pieces is a series of seven booklets by Dr. John W. Reid, entitled "My Time Is My Time." However, even the best pieces are useful chiefly in conjunction with a broad retirement training, where they serve well as subjects for discussion groups. But to hand an employee this literature on his sixtieth birthday, and consider him prepared for retirement (and our duty discharged) is like handing a bees-and-flowers pamphlet to the first-year high school student who finds herself two months pregnant.

RESIDENCE

J. S.'s home is the worst possible for his retirement—an elaborate four bathroom house located in an expensive suburb. The gardens and lawn are in beautiful but static perfection—nothing to plant, nothing to watch develop; a "lawn boy" does the work, just as a series of them have done for 25 years. J. S. is trapped in this house, as finally as a fly in an aspic salad. In a completely changed life situation his home, like himself, belies any vestige of change.

Positive Approach—Residence location is a retirement factor in which early consideration and advice are important. In any change of residence after age 35 the employee should consider the factor of suitability for retirement, or at least plans should begin then toward the ultimate retirement residence.

A friend of the author's on limited income did an excellent job of selecting his retirement location. Six years prior to retirement he and his wife began utilizing vacations to find their spot. Three years later they decided on a North Carolina mountain town, where they purchased some acreage. Then they spent vacations there, becoming acquainted with the townspeople; also during this three years they had a subscription to the local newspaper. Some months prior to retirement the wife left to supervise the beginning construction of their small home. By the time of their big move their house was ready, and their interests were already rooted in the new community—a beautiful example of radical change by gradual transition.

Since no two retirees have the same desires and requirements for retirement residence, each case will be different; nevertheless, certain generalities hold and certain pitfalls must be avoided in every case. If the situation allows, there are advantages to the retiree remaining in his own locale, near friends and family. But if other factors necessitate change, there are advantages in a southern location—older people enjoy better health in a mild climate, particularly if there are cardiac or arthritic problems, and lower living costs due to less heating and clothing expenses are important to retirees of low income.

Neighborhood is all-important. A keeping-up-with-the-Jones neighborhood can wreck retirement, as much emotionally as financially. Nor is a neighborhood exclusively of elderly retirees desirable. An alert 86-year-old returned from a Florida city with the comment, "Never again for that place! All those old people got on my nerves!"

A location affording a large amount of land offers advantages, and the longer before retirement the move is made, the better, as gardening and structural projects can be already in development by retirement (i.e., the interests already established).

Particularly for the employee of vigorous health, developing gardens and planting trees is desirable; these off-the-land projects offer excellent postretirement interest and activity, and some of them may be used financially.

One residence pitfall should be emphasized—moving into the home of a son or daughter. Emotionally, this is the worst mistake the retiree can make. No two generations of a family can live as happily together as they can apart, and usually they can't live together at all. This factor warrants any financial or other sacrifice necessary for the retiree to maintain a separate home. Let the man or woman who doesn't believe this, or who still "just wants to try it," ask this question: "How would I have liked to live with my parents?" Answer this question honestly, and you have answered whether or not you should move in with your son or daughter. Such a move usually ends in an emotional crisis, with the retiree and his wife moving out, blaming the in-law for having "turned our child against us."

COMPANY PUBLICATIONS AND ACTIVITIES

J. S. since retirement has taken no part in company activities, nor has he received any company news publications (which would be meaningless to him anyway since retirees are never mentioned).

Positive Approach—Every possible connection with retirees should be maintained by company papers and activities. Company news publications should carry frequent accounts of activities, hobbies, and accomplishments of retirees, preferably illustrated. These should be scattered through the regular news, not relegated to a separate section which can too

easily become a "Has Been's Corner." Retirees should be invited to all company social activities, such as picnics, plays, exhibits, and holiday parties.

CONSULTING WORK

J. S. would appear to be a natural for consulting work. Actually he has become so one-tracked that he is quite out of date, and no longer holds the confidence of his associates. Thus his efforts after retirement to obtain consulting work were fruitless. (He had given the matter no thought prior to retirement.)

Positive Approach—Many retirees count heavily on consulting work both for emotional outlet and for financial gain. Such work is open chiefly to those who have been in middle or upper management echelons, though there are exceptions, both ways. In J. S. we see a top echelon man who made it impossible for himself to do consulting work. In contrast is a friend of the author's at a lower management level, a "files and records specialist" who all his working life has been interested in people and has been recognized as one who really enjoyed helping associates. To date, three months prior to retirement, he has had three offers of consultation work. Again we see the advantage of broad interests, without which consulting work is difficult to do if obtained.

Consultation work has several advantages: (1) The hours and amount of time can be shaped to the consultant's desires; (2) it keeps the consultant up to date and in contact with his work; (3) it offers the emotional support of having his opinion sought, respected, and paid for—important for maintaining his confidence that he is still worth something. This factor is often more valuable than the money itself, and it holds true for anything for which the retiree is paid, from consulting to selling potatoes he has raised.

The possibility of the retiree's continuing as consultant to his own firm following retirement is too infrequently considered and utilized, although the advantages both to him and to his firm are quite obvious in such an arrangement.

But consultation, like all the previously mentioned arrangements, does not just happen. It must be planned ahead. The following questions must be answered by the man anticipating consultation work in his retirement plan: What part of my present activity and experience will be sought in consultation? To whom will it be of value? How can I *now* begin to make and strengthen contacts necessary later? What preparation should I get now (e.g., public speaking, business writing, organization study)? What record of present activity should I be keeping?

In concluding our thoughts on retirement training, we are tempted to gaze into the crystal ball. Is it not probable, in a period when trained personnel promises to be at a constantly increasing premium, that experience with retirement training will show us ways of tapping the reservoir of potential talent presently wasted in our retiree population? Will we not tomorrow learn to overcome the impracticalities which would today appear so great, if one were to suggest periodic return of retirees to former work areas in order that their opinions concerning current problems might be obtained?

Summary

Industry has produced for man a new and lengthening period of life—retirement—but as yet neither man *nor* industry has learned how to use it constructively.

The lonely idleness and emotional devastation of most retirees today proves that successful retirement requires more than a fishpole and a monthly check, the annuity advertisements notwithstanding.

Retirement is potentially man's happiest, most carefree period, but it requires long-range vision and realistic training to make it so. Such a long-range view and a realistic industrial retirement-training program are outlined; it is the author's conviction that both man and industry can profit immeasurably from them.

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Topical Review

Mercury Toxicity from Industrial Exposure

A CRITICAL REVIEW OF THE LITERATURE—PART II

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Part 1 of this two-part Review, containing References 1-67, was published in the July issue, pages 337-344.

Pathology

As noted earlier, the first recognizable manifestations of mercury intoxication result from interferences with the enzyme systems that are essential to cellular metabolism. As the degree of intoxication increases, morphological changes occur. Since subacute and chronic intoxications rarely cause death, however, the published reports of their associated pathology are meager and for the most part unclear, defects which unfortunately carry over to the report of animal experiments. Furthermore, such uncertainty is due partly to the technical difficulties of studying the kinds of toxic changes in nervous tissues that are produced by mercury. For these reasons a description of the pathological features of mercury intoxication must be fragmentary and largely based upon what can be learned from the picture of acute intoxication.

Oral—The oldest observation of pathological findings in industrial mercurial intoxication concerns changes of the oral mucosa. Gingivitis, and less frequently, stomatitis of the ulcerous type, were described early,[50] the latter having been observed again recently in mercury refinery workers.[20] The histology of these changes is described in terms of epithelial hyperplasia, edema and mononuclear infiltration of the submucosa;[68] and x-ray studies may reveal alveolytic changes.[69, 70]

Renal—The renal involvement, until recently a matter to be questioned as a feature of chronic intoxication,[1, 71] is now rather clearly documented by several clinical reports[4, 17, 18, 19, 72, 73]; and it is considered a not uncommon finding, reproducible in animals subjected to chronic exposure.[34] Nevertheless, its postmortem documentation in humans with chronic mercury exposures is practically not available. Inferences derived from clinical findings may lead to two different concepts. The first of these considers the chronic kidney lesion to be a mere attenuation of the acute change produced by mercuric chloride,[19] in which albuminuria, red cells, and casts point to an ill-defined, nephrosis-like picture. The second concept deals with renal changes of the arteriosclerotic or arteriolosclerotic type,[74, 75] but clinical observations are neither sufficiently detailed nor extensive enough to permit a definite conclusion in this matter.

Nervous—The pathology of the human nervous system consequent upon mercury intoxication has been described adequately only in conjunction with exposure to the alkyl derivatives. The gross changes produced by these compounds consist of cerebellar and, to a lesser extent, of cerebral cortical atrophy. Microscopically, a selective involvement has been described in man in the granular layer of the cerebellum, gangliar cells, and the posterior columns. Diffuse changes of cellular stainability were observed in these circumstances throughout the central nervous system,[17] very similar to the lesions described in monkeys exposed to methyl mercury compounds.[76] Peripheral neuritis, reported quite uncommonly, is associated with scattered demyelination.[77]

Endocrine—In regard to the endocrine system, pituitary and adrenal degenerative changes are reported, with descriptions of gross morphological as well as histological lesions. Changes in volume, shape, and color, evident at gross inspection, are accompanied by altered stainability and abnormal cellular arrangement. In one case eosinophil hyperplastic changes were noted in the hypophysis.[78]

Skin—Dermatitis is a finding independent of systemic poisoning, and it has been ascribed to

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exposures to almost any compound of mercury.[51] Mercury nitrate, to which hatters may be exposed during the manipulation of felt, may induce erythematous, papular, and vesicular lesions which go on to lichenification and fissuring.[11] Blisters and ulceration are reported as resulting from contact with the more irritating mercury compounds, such as fulminate ("powder holes") and alkyl derivatives.

Respiratory—Respiratory involvement resulting from intensive exposure is rare, but does occur.[13] It may reach the severity of necrotic changes of an erosive bronchitis, with bronchiolitis and interstitial pneumonitis.[6]

Bone Marrow—Bone marrow seems to remain unaffected by mercury. Although mention has been made of increased hemoglobin value and erythrocyte size,[79] other clinical and experimental observations have failed to reveal any statistically significant abnormality in this regard.[80, 81]

Clinical Aspects

Three signs have characterized, traditionally, the diagnosis of industrial mercurialism: gingivitis, tremor of the extremities, and emotional instability. The clinical course includes an insidious onset and a slow and progressive evolution. Acute features are possible, however, when the occupational exposure to respirable inorganic compounds is intensive, or they may result from inhalation of small quantities of organic mercurials, which, as seen previously, may produce intoxication quickly. Therefore, we have to conclude that mercurialism, although a chronic intoxication most of the time, may occasionally assume the features of an acute syndrome. The diagnostic triad does not appear in a fixed pattern. Any one or two of the signs may be present without the others, and in varying degree, in which case the diagnosis becomes relatively uncertain. This is especially so when some other clinical entity is simultaneously present.

Digestive—Gingivitis has been repeatedly questioned as a reliable indicator of mercury intoxication. Poor oral hygiene is commonly invoked to explain this disturbance in preference to the implication of mercury. It seems reasonable to conclude that mercury may aggravate or, at least, favor and maintain preexisting trophic changes primarily induced by lack of proper mouth care. It seems also acceptable that workers who have adequate oral hygiene and who are significantly exposed to mercury rarely exhibit gingivitis. Salivation in excess of normal has frequently been reported, although the workers often label as salivation what is really a metallic taste. Decreased appetite, constipation, diarrhea, and dyspepsia, the frequent complaints of exposed workers with mercury intoxication, may well be due to minor trophic changes of the mucosa and possibly the nerve supply of the gastrointestinal tract. Actually such complaints never reach the intensity encountered in the gastroenteritis of acute oral poisoning. Several observers tend even to discredit minor gastrointestinal complaints as a reliable manifestation of mercury toxicity.

Renal—Renal involvement, as manifested by albuminuria, casts, and (sometimes) red blood cells, is not an uncommon finding in chronic absorption of inorganic as well as organic (alkyl) mercurials. Usually it constitutes a mild and reversible disturbance. As stated earlier, the nephrosclerotic type of renal involvement has not yet been defined sufficiently to allow a satisfactory clinical description at this time.

Nervous—Although neurological changes are somewhat different when caused by alkyl compounds than when caused by the element or inorganic mercury compounds, a general description may apply to all instances. Poisoning by the alkyl compounds is apt to be subacute in its onset and intensity, and usually presents ataxic and sensory changes; whereas cases caused by mercury element or its inorganic compounds have an insidious onset and usually are characterized by hyperkinetic changes.

Muscular tremor is the eloquent sign of mercurialism. It is both static and intentional, although the latter is the one of which the patient first becomes aware. Five degrees of tremor have been described:[11]

1. Slight static tremor, evidenced with the arms outstretched and the fingers spread and often not manifest to the patient himself. It does not disturb to any extent a satisfactory muscular activity.
2. Static tremor of greater degree associated with early intention tremor, moderately affecting delicate muscular activity.
3. Static and intention tremor which prevents or seriously disturbs delicate muscular activities (writing, shaving, holding a glass).
4. Tremor inducing conspicuous difficulties in gross movements.
5. Generalized intense tremor, preventing daily living activities ("concussio mercurialis").

The most advanced degrees of tremor are not infrequently accompanied by myoclonic movements, which may be limited to a limb or may involve the total body ("shakes"). A characteristic of any degree of tremor is its worsen-

ing induced by the observation of a stranger or a doctor.

Sensory involvement, as numbness, paresthesia, and, less frequently, hypesthesia of extremities, tongue, and lips, may be present, especially as a result of organic mercurial exposure.

The well-known mercurial erethism is described in terms of irritability, sudden changes of sociability, reduced attention, and insomnia. On more than one occasion such changes, together with sensory disturbances, have suggested the diagnosis of hysteria.

Ataxia, dysarthria, and sphincter incontinence are present in severe organic mercurial intoxication. A true peripheral neuritis, with involvement of both sensory and motor fibers, is rather exceptional.[77] Headache, dermographism, and hyperreflexia have been described but possess such an equivocal clinical meaning that they are considered of little help in the diagnostic elaboration.

Eyes—Several observers have described restriction of visual fields, in both organic and inorganic mercurial exposure.[17, 20] The change is attributed to central atrophy. Crystalline lens discoloration, detected for the first time by Atkinson, has been reported by other observers.[82, 83, 84] It may be observed with a slit-lamp as a brownish reflex on the anterior surface of the lens and is considered a rather early change of mercury intoxication.

Ear—The inner ear, the acoustic as well as the vestibular section, apparently may be involved *in toto,* according to Krajina;[85] but this finding has not been confirmed by others. However, mention of isolated hearing impairment has been made in connection with exposure to alkyl derivatives.[18]

Thyroid Dysfunction—There is some resemblance between the signs of hyperthyrodism and mercurialism, as suggested by tremor, dermographism, and emotional disturbance. But no evidence exists of a direct thyroid involvement in mercury intoxication, according to the largest epidemiologic inquiries in this respect.[10, 86] Neither glandular enlargement nor increased metabolic rate is present with a higher frequency in intoxicated subjects than in the general population.

Diagnostic Tests—Because of the insidious character and vague clinical picture of mercurialism, the diagnosis would be more accurately formulated with the aid of laboratory data. However, no highly discriminating tests are available. In a comparison of mercury concentrations in biological fluids, the blood level of mercury seems to be the least reliable. The rapid loss of mercury from the blood stream after absorption has been clearly demonstrated in experimental animals.[34, 48] Even if levels in exposed persons are frequently found to be higher than those in nonexposed,[87] the oscillation of this value in different individuals and in various exposures precludes its practical use.

The alkyl mercury derivatives are said to appear rapidly in cerebrospinal fluid.[88] The determination of mercury content in this fluid could theoretically offer a sound index of the quantity localized in the central nervous system. Obviously, though, such a test has little practical application and is mentioned here only for the sake of documentation.

The determination of the quantity of mercury eliminated by the alimentary tract is subject to serious practical limitations. Furthermore, it constitutes but a small percentage of the total elimination.[46] Therefore, the greatest attention has been devoted to the urinary output.

It is well established that the urinary level of mercury of nonexposed persons is close to zero,* as determined by the usual methods of analysis.[89] Among persons with apparently equal and consistent exposures there is considerable variation in the urinary mercury level found not only among different individuals but within the same individual on successive days; and those with signs of intoxication are apt to present lower urinary levels than are found among the nonintoxicated.[7, 10] Because of these variables, the establishment of a diagnosis of mercury poisoning in a given case should be based primarily upon history and physical findings, with secondary reliance on the urinary mercury level. There is, however, reasonably good correlation between the degree of mercury exposure of *groups* of workers and their urinary mercury elimination, in which circumstance the response of individuals is concealed in the average, or group, response.[90] When workers are systematically followed in this manner, a concentration of 0.1 mg Hg per liter of urine may be taken arbitrarily as an indication of a hazardous exposure.[91]

Prognosis—In cases of mild intoxication the symptoms of mercurialism may regress significantly after exposure ceases. In a series of 135 cases reported by Baldi, Vigliani, and Zurlo[11] the great majority (79%) of the patients affected with slight mercurialism showed a conspicuous improvement in the course of four or five years after the exposure ceased. Patients with more advanced degrees of intoxication, however, are less likely to show improvement.

*Attention should be paid to accidental food contamination and mercurial therapy, since both may account for significant mercury excretion.

In the same clinical survey, only 15% of the patients with marked manifestations of mercurialism improved in subsequent years. The outlook for those most seriously affected is even worse. The case described by Hunter[20] may serve as a striking example. Fifteen years after an encephalopathic syndrome caused by a few months of exposure to methyl mercury compounds, the patient was still unable to resume any sort of work because of persistent ataxia, tremor, and astereognosis.

Therapy—While the acute intoxication is apparently helped by the dimercaprol (BAL) treatment, at the present time there is no satisfactory therapy of chronic mercurialism. In such cases, the use of dimercaprol has not only been of doubtful effectiveness,[19] but it is even considered harmful by some writers.[20] Nevertheless, there are reports which favor its use in chronic intoxication.[92, 93] In this country, Bell, Gilliland, and Dunn[31] were able to increase significantly the urinary output of mercury by the administration of dimercaprol in a case of chronic intoxication. The chelating agent edathamil (ethylenediaminetetraacetic acid; EDTA), tried in the same case, did not produce any positive effect at variance with the results obtained by others.[94] In animal experiments, however, the use of dimercaprol does not appear to induce regular urinary elimination. According to Borghgraef and Pitts,[45] the simultaneous addition of dimercaprol to mercury administered experimentally to animals will increase its binding with cellular moieties other than those of the kidneys. Actually, the urinary elimination of mercury in response to dimercaprol treatment seems to depend largely upon the particular mercury compound involved and upon the urinary pH.[95] In alkaline urine dimercaprol induces a significant urinary excretion of mercury, given as mercury-cysteine, where as in acid urine this effect is not present. On the basis of a study of cellular respiration cited before,[67] it was concluded that the inhibition of glucose uptake by mercury can be reversed by monothiols or dithiols. However, where the metal has penetrated the cellular membrane, its effect on cellular respiration cannot be reversed by the thiols. One would not expect, therefore, that the administration of dimercaprol some time after mercury is absorbed would significantly influence its elimination from sites of deposit.

A recently synthesized compound, N-acetyl-*dl*-penicillamine, has been suggested as an antidote for mercury intoxication. It is packaged for oral administration. The first experimental studies suggested that such an antidote is less effective than dimercaprol in acute mercury intoxication.[96] Its value in chronic mercurialism is not yet known.

In summary, it must be said that a definitive treatment of chronic mercury intoxication has not been developed as yet. An appropriate treatment probably will require more than one scheme, considering the intermediate metabolic differences of various mercury compounds.

Prevention

Clinical Control—Clinical observations of use in the early detection of cases are as follows:

History
1. Oral and intestinal complaints
2. Nervous complaints, especially tremor in performing fine movements, sensory changes (numbness, etc.) and incipient incoordination (buttoning, shaving)
3. Metabolic changes (weight, appetite)

Physical examination
1. Oral changes
2. Neurological changes
3. Eye finding (Atkinson's sign and constriction of the visual fields)

Laboratory tests
1. Urinary abnormalities
2. Urinary mercury excretion

An adequate history should focus principally on nervous system changes, although changes of weight and appetite, and digestive disturbances may be considered also as an indication of incipient mercurialism. Irritability and tremor—evidenced by handwriting changes, difficulties in handling a tumbler of water and shaving—are good indications of toxic mercurial effects. Paresthesias, referred to as numbness or tingling of the extremities, lips, or tongue are frequently present, particularly in organic mercurial exposure, but may be encountered in inorganic and elemental mercury intoxication as well.

The examination should give emphasis to the nervous system for evidence of tremor, sensory disturbances, visual field change, ataxia, and the rarely occurring dysarthria. The simple tests of writing and drawing will be very helpful in revealing fine intention tremor, especially if they can be compared with samples previously obtained.

Useful laboratory tests are limited to routine urine analysis for the presence of elements of toxic renal damage and to the determination of the level of mercury concentration (see Mercury Determination in Air and Biological Specimens: Biological Determination).

Environmental Control. Effective prevention is dependent upon the maintenance of safe conditions in the production and use of mercury.

Good ventilation, airtight distillation equipment, and cleanliness of benches and floors are the main requirements. Floors should be washable, and sinks should have collection traps. Sulfide solutions for the cleaning of work surfaces are suggested, but a dichromate solution seems to be even more efficient.[97] In order to check the efficacy of the control measures, it is necessary periodically to analyze the air in the breathing zone of the workers as well as the solutions handled by them.

Mercury Determination in Air and Biological Specimens

Air Determination—Several methods are available for the determination of mercury in air. Extensively used for simultaneous sampling and analysis is the mercury vapor detector, which utilizes a simple ultraviolet spectrophotometric principle. This instrument measures only mercury vapor and therefore is not suitable to assess mercury which is present as particulate matter or dispersed as an aerosol.[9] A second, direct-reading, instrument is the selenium sulfide paper detector, which is adequate for prolonged sampling only if the reading of the blackened paper is accomplished by means of a densitometer.

The standard impinger method, devised by Barnes,[98] uses a sampling solution of iodine in potassium iodide. A pink-to-orange color, indicative of the presence of mercury, is developed by subsequent treatment with copper sulfate and sodium sulfide.

The United Kingdom Atomic Energy Authority collects samples in an acidified solution of potassium permanganate, using three absorption bublers in series; and the sample is subsequently titrated with standardized dithizone solution.[99] The dithizone method of analysis[100] has wide application to samples collected by a variety of methods.

The electrolytic method has been accepted since the first suggestion of Stock[89] and is presently used routinely by the Massachusetts Division of Occupational Hygiene.

Biological Determination—A rapid microflame spectrophotometric determination of mercury was proposed by Lindstrom[101] and considered particularly suitable for food products.

Spectrographic methods are probably the most accurate procedures for analysis of biological materials in general for mercury content, but they require expensive laboratory equipment.

The dithizone method, in spite of objectionable features, is still the most commonly used in this connection. One drawback is the interference of different trace metals with the analytical procedure. Furthermore, the heat required to free mercury from the organic material is likely to induce a significant loss of the element. Care should be taken to maintain the temperature of the digesting bath at a minimum in order to avoid the mercury volatilization. Accurate control of reagents and solutions is an indispensable factor to avoid interference by different metals.[100]

Summary

This review aims to provide a synthetic description of mercury intoxication, the conditions of exposure necessary to produce this condition, and the related clinical features. For this purpose, an extensive bibliographic review of literature was necessary, giving emphasis to the publications of the past 20 years.

The biochemical lesion of mercury in the organism seems to consist always of an enzymatic inhibition. Various enzymes could be involved in human intoxication, but the state of our knowledge in this regard is far from satisfactory.

A series of three variables are identified as the main factors in the onset and localization of the toxic action; namely, the amount and rate of mercury absorption, the chemical characteristics of the compound, and the individual susceptibility of the exposed subject. Early diagnosis of mercurialism is still dependent upon a clinical examination which emphasizes a search for typical central nervous system changes. Eye changes are sometimes contributory, and routine urinanalysis may reveal involvement of the renal parenchyma. Levels of urinary excretion of mercury should always be interpreted carefully and on the basis of several samples.

There is no satisfactory therapeutic procedure for chronic mercurialism at the present time. Preventive measures as well as methods of mercury determination in air and biological material are outlined.

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Industrial Medical Association

THE PRESIDENT'S MESSAGE

ROBERT E. ECKARDT, M.D.

DURING the Rochester meeting, many decisions were reached by your officers and directors which make it possible for our Association to continue operating during the coming year. Some of these were more or less routine and, although not unimportant, need no further elaboration. Others, however, should be brought to the attention of our membership for their general knowledge and consideration.

One important decision reached by the Board of Directors, after a plea by our editor, Dr. A. G. Kammer, and with the recommendation of our Journal Committee under the chairmanship of Dr. Arthur Peterson, was to increase the text section of the JOURNAL OF OCCUPATIONAL MEDICINE eight pages per month. It was necessitated by the wealth of good editorial material and abstracts which have been denied publication only because of lack of space for them in the JOURNAL. The Board of Directors believes that our JOURNAL is the single most important service we render to our membership, and that anything we can do to improve it is improving our service to the membership. In addition, our Journal Committee has recommended that more news items about our members and our component society activities in the JOURNAL would be of interest. This is endorsed by our officers but requires individuals and component societies to forward to the publication office, *in sufficient time*, items of this nature. This page, for instance, is being written *June 10*, for inclusion in the *August* issue.

The second important decision of our Board was to recommend a dues increase of $10 for members and fellows. Three years ago our Finance Committee pointed out that this would be necessary if our Association were to be able to continue and enlarge its services to our members.

Many worth-while committee and association activities, such as committee studies and the publication of a new up-to-date roster of members, have had to be put into abeyance for simple lack of funds. To rectify this, a dues increase is essential. Your Board realizes that dues increases are not popular but hastens to point out that we have only had one $5 dues increase, despite the inflationary trends and increased costs all around us. Since an increase in dues must be effected through a change in the By-Laws, which can only be voted on at our April, 1961, meeting to be effective Jan. 1, 1962, there is ample time for the Board to receive the ideas and recommendations of the component societies prior to any definitive actions on this recommendation. A representative of the Board has been asked to present and discuss this recommendation with each component and thus to let the Board receive the recommendations of all the components before presenting its final recommendations to the membership at the April, 1961, meeting. Direct members are invited to send their comments and suggestions directly to me in keeping with the democratic traditions of our organization.

Our Committee on Industrial Medical Practice has designed a questionnaire to be sent to all members, to determine the scope of industrial medical programs. Distribution of the questionnaire was held up because of lack of funds for adequate analysis of the results. Means are now being developed to overcome this difficulty, and professional help and guidance in the design and ultimate analysis of the questionnaire have been volunteered. It seems likely that about the beginning of next year the questionnaire will be distributed to our total membership. When the Council on Occupational Health distributed a similar questionnaire to

our membership several years ago only 7% were returned, a number too small for reliable conclusions. It is my urgent plea to each and every member that when you receive the questionnaire you take the time to answer it fully, and accurately, and return it promptly so that this project can be successful. We shall need your help. *Please* let us have it.

Finally, our President-Elect, Dr. Rowntree, and our Managing Director, Clark Bridges, are working diligently on a means of printing a new directory of our membership. Such a directory has great value to our full-time members who may be looking for a part-time man for referral work. Conversely it is of value to our part-time men by bringing them referrals. As such, therefore, it is an important membership service that, except for budgetary considerations, should be up-dated at frequent, if not yearly, intervals. It is our hope that the increase in dues will make this important goal also attainable.

Book Reviews

RADIATION BIOLOGY AND CANCER: A COLLECTION OF PAPERS PRESENTED AT THE TWELFTH ANNUAL SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH AT THE UNIVERSITY OF TEXAS. M. D. Anderson Hospital and Tumor Institute. Price, $8.50. Pp. 486. University of Texas Press, Austin 12, Texas, 1959.

During the past 25 years, radiation research and cancer research have had a closely parallel development. Radiation exposure to experimental animals has been a convenient, easily controlled, and satisfactorily measured method for inducing various tumors. It has provided geneticists with a precise method for producing mutations in genetic material, the effects of which could be closely investigated by breeding and cytological studies. Labeling hydrocarbon compounds with radioisotopes has enabled biologists to follow and understand many dynamic processes which previously could be studied only statically.

This book is a collection of papers presented at the Twelfth Annual Symposium on Fundamental Cancer Research held in 1958 at the M. D. Anderson Hospital and Tumor Institute at Houston, Texas. Many of the papers are summaries of works to date by prominent groups and individual investigators from many laboratories. A number of more detailed reports of recent work done at the Anderson Hospital of the University of Texas are also included.

The probability that somatic mutation plays an important role in causing neoplastic change is either openly discussed or implied in a number of the papers. Dr. W. J. Burdette, of the University of Utah, feels that somatic mutation must be admitted as a possible, but not probable, cause of cancer. Drs. Haas and Doudney, of the University of Texas, who have studied DNA synthesis in cells exposed to ultraviolet light, feel differently. They have found that nucleic acid precursors must be exposed to radiation in order for an increase in induced mutations to take place. They also note that with each technical advance more carcinogens have been found to be mutagenic. Studies by Dr. Stanfield Rogers, of the University of Tennessee Memorial Hospital, indicate that the neoplastic changes in pulmonary cells that are induced by ultraviolet light are also dependent upon damage to genetic material rather than chemical intermediaries.

Dr. Faith Furth, of Children's Cancer Research Foundation, states that "irreversible hereditary alteration in cells and indirect hormonal effects are the most powerful factors in the induction of neoplasms by radiation." Dr. A. Kirschbaum, of Baylor University, concludes that multiple factors are involved in the induction of mouse leukemia. If a filtrable virus is the immediate primary cause, its action may be augmented by x-ray exposure, which, in the final analysis, may be as important as the so-called "primary" agent. Unfortunately, the chief obstacle in investigating somatic mutation is the fact that somatic cells are diploid and reproduced by mitotic division. If only somatic cells mated like germinal cells!

A new and exciting field in radiation biology, which has many implications for clinical medicine, is the study of organ transplants following lethal radiation dose. Great effort is now being expended in trying to understand the fundamental mechanisms of secondary disease. This causes weight loss and late death in experimental animals after apparently successful transplantation of homologous or heterologous bone marrow. A much more complete understanding of the basic immunochemistry involved will be necessary before this problem can be solved. Thus, radiation biology research may uncover the secrets of antigen-antibody reactions. This may be the key to understanding many diseases in which some form of immune reaction appears to be important.

How can the specialist in occupational medicine use this book? Certainly not just to "dress up" his library because radiation biology is a fast moving field of research. Since this is not a textbook or a collection of broad reviews, it will have a somewhat limited use as a reference book. Physicians who have a special interest in chemical carcinogenesis should be interested in this approach

to cancer research. Those who do not have a special interest in radiation biology or cancer may still enjoy exploring in this important field of research. They will find that digging into, for example, Dr. John Trenton's paper on the "Consequence of Bone Marrow Induced Radiation Recovery" is a challenging but satisfying experience.

—T. A. LINCOLN, M.D.
Carbide & Carbon Chemicals Co.
Oak Ridge, Tenn.

TRAUMA. Harrison L. McLaughlin, M.D. Price, $18.00. Pp. 784, with 407 illustrations. W. B. Saunders Company, W. Washington Sq., Philadelphia 5, Pa., 1959.

This book, with its eye-catching single-word title, should be of value to all physicians called upon to treat people injured on the highway, on the farm, in the home, or in the factory. There has been a long-felt need for a book on the broad subject of trauma as it occurs in the civilian. The value of the book can be appreciated when we consider that trauma causes morbidity and death in more people between 1 and 50 years of age than does any other disease. The disease states produced by trauma cross the lines of all specialties. Understandably, a composite group of authors was needed to write this book. Dr. McLaughlin is well qualified to bear the burden of senior authorship and to coordinate the work of the associated authors. He has succeeded in doing both.

The material is very well organized, with excellent choice of illustrations, the latter stressing the problems and principles of treatment rather than cluttering up the book with end-results. The index seems adequate. The senior author has written 12 of the 25 chapters; these are uniformly excellent. His material is presented in a manner and language and with a choice of information of value to those for whom the book is written. Most of the associated authors have come up to the standards set and help in achieving his goal.

The book is divided into five main sections. The first section, "General Considerations," covers the pathophysiology of trauma and the principles of treatment based on the local and constitutional response of the body to injury. Not forgotten is a discussion of the emotional response of the person to injury. Covered quite thoroughly in this section are shock, the initial care and transportation of the injured person, the person with multiple injuries, infection and antibacterial agents, thermal trauma, vascular injuries, and the principles and treatment of fractures: preparation of the patient for treatment, timing of reduction, and the problem of open fractures. These first five chapters are excellent. They offer the foundation for discussion of the more specific injuries which are covered in succeeding chapters. This section should be required reading for senior medical students, interns, and residents in all specialties.

The upper and lower extremities are considered in sections two and three, respectively. Injuries to the bones and joints are very well covered. Stressed by the authors is the fact that fractures in children are different from those in adults from the standpoint of recognition, treatment, healing, and end-results. The chapters on the shoulder, wrist, and ankle are excellent. Injuries to the soft tissues of the extremities could have been considered in more detail.

Section four, "The Trunk," covers injuries to the abdomen, pelvis, chest, vertebral column, lower back, and cervical cord and its adnexa. The chapters on the chest and lower back are excellent. Discussion on the cervical cord and its adnexa is very good. The chapter on injuries to the abdomen is the least informative in the book. Except for the bladder, injuries to the urogenital tract are not touched.

The fifth and the last section covers injuries to the head and special senses. The first chapter, on injuries to the brain and skull, is one of the best and comes up to the standards set by the senior author. The remaining chapters, on injuries to the maxillofacial region, auditory apparatus, nose and paranasal sinuses, and eye, complete the book. They are done well. Missing is a more complete discussion of treatment of soft-tissue injuries of the face.

It is the reviewer's opinion that the author has succeeded in accomplishing what he has set out to do, namely, publish a book on trauma which would offer information and would have appeal to the doctor who sees the injured individual first. There are a few weaknesses, which are found in any book, particularly in a first edition. These shortcomings could be corrected in subsequent editions. This work should be carried on. There could be more coverage of intra-abdominal injury, including the urogenital tract, and also injuries to the soft tissues in specific areas, i.e.: the skin and subcutaneous tissues of the face and hand—and nerve and tendon injuries.

This book is recommended for house officers, students, and those dealing with injured people in the broad sense. The book should be in the library of every factory dispensary and every hospital. The subject of trauma will play a more prominent part in the practice of almost every physician in years hence.

—IRWIN SCHULZ, M.D., Milwaukee, Wis.

TEXTBOOK OF TOXICOLOGY. Kenneth P. DuBois, M.Sc., Ph.D., and E. M. K. Geiling, Ph.D., M.D. Price, $6.50. Pp. 302, with index. Oxford University Press, 417 Fifth Ave., New York 16, N. Y., 1959.

Industrial toxicology has expanded so rapidly that it is no longer possible to include adequate coverage of the subject in the formal course in pharmacology. Some academic institutions have recognized this need by introducing courses and graduate training programs in toxicology. This volume is intended as an introductory textbook presenting the essentials of toxicology for medical students, graduate students, and advanced undergraduates in the biological sciences. The authors have utilized their

experiences of the past 15 years in the teaching of a toxicology course as the basis for the organization of the textbook and the selection of the subject matter.

The introductory chapters (1-3) are devoted to the History, General Principles, and Medico-Legal Aspects of Toxicology. The Air-Borne Poisons (Gases and Dusts), Corrosives and Phosphorus, and Metals are discussed in chapters 4 to 9. Radiation Hazards, Alcohols and Solvents, Pesticides, Plant and Animal Poisons, Household Poisons, and Toxicological Analysis constitute the chapter headings of the rest of the book. Selected references are listed at the end of each chapter, and an index is provided to cover the subject matter treated in the text.

The authors have succeeded admirably in attaining their primary objective of presenting an introduction to the subject of toxicology. The book is well organized and written in a lucid, direct style. Details have been excluded in order to emphasize basic principles and salient points. The volume is not intended to be a source of toxicity information for practicing toxicologists or physicians in industrial medicine. The information presented on specific chemicals is generally available in other well-known sources.

—HORACE W. GERARDE, M.D., Ph.D.
Esso Research and Engineering Company
Linden, N. J.

PROTECTION IN DIAGNOSTIC RADIOLOGY. Edited by B. P. Sonnenblick; introduction by C. B. Braestrup. Price, $7.50. Pp. 346, with illustrations. Rutgers University Press, 30 College Ave., New Brunswick, N. J., 1959.

Protection in Diagnostic Radiology is an integrated collection of the better articles in this field, which have been published largely in specialized journals throughout the world. These articles, presented in orderly sequence, indicate the nature and extent of the problem, the amount and major sources of exposure to patients and personnel, the significance of maximum permissible dose levels, and methods to increase protection.

Surveys indicate a considerable lag in putting into practice a few relatively simple procedures which involve filtration, coning, fast film and gonad shielding. These could greatly reduce exposures to somatic and germinal tissues. As would be expected, the specialized radiologists have made much greater progress in protection than have the nonradiologists, to whom the use of x-rays is only incidental to their regular professional activities. This latter group includes physicans, dentists, osteopaths, veterinarians, chiropractors, podiatrists, and their technical assistants. The book brings to this group a wealth of material regarding the need for protection and methods of protection, and indicates where expert assistance may be obtained.

Industrial physicians should have firsthand knowledge in this field, for they either operate a diagnostic installation or secure such service for the employees under their jurisdiction. While other sources of radiation exposure to individuals and whole populations are discussed, it is shown that the greatest source of exposure is from diagnostic radiology and that this can be greatly reduced without compromising the excellence of the service.

This book is a vital aid in the urgent campaign to alert all those who operate radiological equipment to use it with maximum benefit to patients and minimal exposure to patients and personnel.

—W. DAGGETT NORWOOD, M.D.
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Hanford Atomic Products Operation
General Electric Company
Richland, Washington

TOTAL SURGICAL MANAGEMENT. James D. Hardy, M.S., M.D., F.A.C.S. Price, $9.50. Pp. 292. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, N. Y., 1959.

This short, 277 page book on Total Surgical Management is just that and will be found of particular help to the house physician. It deals with many specific conditions, as well as the diagnosis and preoperative, operative, and postoperative care of all the broad groups of surgical patients. In addition, many features such as fluid therapy and nutrition, blood replacement, bleeding disorders, wound management, order writing, the particular problems of infants, safe use of anesthesia, and the psychological consideration of the surgical patient are discussed. Obviously, the author cannot cover each of these items in great detail.

He has throughout, it seems to the reviewer, sought to pass on to the younger surgeon the benefit of his own experience over the years. In the discussion of each problem, Dr. Hardy points out its unique pitfalls the avoidance of which are usually learned by long experience, some of it unfortunate. Many of these could be avoided throughout a lifetime of surgery if the student would carefully read the admonitions contained in this small volume. The short case histories frequently used to illustrate dramatically these points are particularly delightful. These are the "pearls" which were gathered by the attentive house doctor during the several years of experience under the professor's watchful tutelage. Though this is the great attraction of the book, one hastens to add that the general material is also factual and sound and seems to represent the author's experience as chairman of a surgical department in a teaching hospital. It is short, reads very easily, and will be enjoyable to any surgeon. Those without great experience will benefit by absorbing the specific information contained therein. The experienced surgeon will enjoy recalling the circumstances under which he himself learned how to avoid these particular pitfalls.

—ROBERT C. COMBS, M.D.
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Editorial

Hippocrates in Industry

OUR ANCIENT oath contains four obligations which are as applicable today as they were in the time of Hippocrates. These are to impart the knowledge and teach the art of Medicine to those who follow; to utilize modern methods of treatment and to exercise the highest degree of judgment and skill; to exercise integrity, refraining from any thought of practice not directed toward healing the sick; and to keep inviolate the patient's right to privacy and, in the broader sense, his dignity as a human being. Let us see how these obligations apply to the practice of Occupational Medicine.

The Obligation to Teach—The industrial physician must instruct his assistant physicians and nurses and encourage first-aid training for employees. He should actively participate in plant safety programs. Since occupational medicine has become a recognized speciality, the physician should offer his services to medical schools which offer this course.

Methods of Treatment—The industrial physician has an ethical obligation to render his most skillful service to employer and employee. He must be familiar with the current medical literature. He should regularly attend conferences, seminars, and courses dealing with his specialty.

The Exercise of Integrity—There is no physician who has not been tempted to change his professional opinion because of personal feelings. Since the industrial physician is a management employee, there is a tendency to view medical problems from a mangement standpoint. On the other hand, he may let his judgment be affected by sympathy for an employee's domestic situation.

There is but one way to maintain integrity in occupational medicine: to have it understood that the medical department is completely neutral, representing neither management nor labor. Neutrality is the basis for employee confidence and respect. Under no circumstances should the medical department be utilized as a tool to rid the corporation of an undesirable employee.

The Patient's Right to Privacy—It is undoubtedly this fourth obligation that creates the most problems. We have always recognized the importance of the doctor-patient relationship. It is that intimate, confidential, personal relationship so necessary to the treatment of human ills.

To gain the confidence and faith of the patient is the goal of any physician. This may be very difficult in the field of industrial medicine, since the physician is not freely chosen by the employee but is management-appointed. In situations where labor relations are strained, the physician's role is doubly difficult because the employee's initial reaction to diagnosis and treatment is apt to be one of distrust. Modern medical practice has witnessed the advent of the so-called "third party" in the doctor-patient relationship. This may be an employer, insurance company, union, or government agency. Usually the "third party" is the one who pays the bills. A question arises: How much, if any, information may be divulged to this "third party"? Hippocrates had no such problem, because "third parties" were unrecognized 20 centuries ago. We must, in justice to the "third party," reconcile his rights with the demands of this portion of the oath.

We feel that the practice of medicine is dynamic and capable of adjusting itself to modern needs without sacrificing its basic ethical tenets. The dilemma caused by the obligation to privacy, on the one hand, and the obligation to the financially responsible third party, on the other, must be resolved.

A solution is to be found in the law governing contracts. The voluntary entrance into a contract by the patient (employee) with a third party (employer, insurance carrier, etc.), the conditions of which include payment of part or all of the medical expenses, carries with it the obligation to provide the third party with the specific information needed to support the disbursement of funds. Usually this means revelation of the etiology, diagnosis, and prognosis of the injury or illness upon which a claim is

based. The industrial physician behaves ethically when he makes known these facts to the employer. Indeed, the withholding of such information would constitute an obstructive act, an interference with the receipt of benefits that are the employee's right.

These, then, are the principles which should guide the industrial physician in applying the Hippocratic Oath to his specialty. Only by maintaining neutrality and by safeguarding privileged communication may he earn the confidence of both employer and employee and thereby render his best service to each.

—Guest Editorial by A. T. HALL JR., M.D.

Information Please

The questions published in this column are edited versions of requests for information that have been received during recent months. The answers have been prepared by one or more competent authorities in the particular area covered by the question. Readers may address questions to the Editor.

QUESTION: *Several textbooks report that the toxicity of toluene and that of benzene (benzol) are similar but that benzol is more dangerous to health because it evaporates more readily than toluene. At the same time one finds that the maximum allowable concentration value for benzene is given as 35 ppm and that of toluene as 200 ppm. It would appear that if the toxicity of the two were the same, they should have the same maximum allowable concentrations. Can this discrepancy be explained?*

ANSWER: Although there have been very few definitive studies concerning the toxicological effects of toluene on man, the evidence which is available indicates that toluene is somewhat less toxic than benzene. The latter is known to have caused serious damage to the blood and blood-forming organs, while the former rarely if ever causes serious hematologic abnormalities. In the light of the knowledge that is available at present, those textbooks which state that benzene and toluene have comparable toxicity are probably in error. The different MAC values more properly reflect the relative toxicity. It should always be borne in mind, however, that commercial grades of toluene often contain appreciable amounts of benzene as an impurity. This fact may have contributed to some of the confusion.

QUESTION: *I have a current problem related to and hence a special interest in the matter of electric shock followed promptly by "indigestion" and discomforture in the chest with symptoms that recurred and terminated in a myocardial infarction about ten days after the accidental electric shock. I would appreciate receiving any information that may be available concerning correlation between electric shock and cardiac muscle damage and/or myocardial infarction in a surviving patient. In addition, is there any information on the possible interrelationship between diabetes and electric shock?*

ANSWER: Present knowledge does not indicate that electric shock is a significant etiologic agent in the development of atherosclerosis of the coronary arteries, although the ability of electric shock to produce cardiac arrhythmia appears well established. Since electric shock can be quite a traumatic experience generally and since it may have effect on the heart specifically, the role of electric shock as a precipitating factor in coronary occlusion and subsequent myocardial infarction cannot be generalized but becomes a matter for careful clinical judgment based on data applicable to the individual case.

If this man recovered from his shock and subsequently within an hour or so developed symptoms or other evidence suggesting myocardial infarction, one would assume that the shock played some part in the development of the infarction, which could well have developed at some later date in the absence of the shock. At the opposite end of the scale, however, one can picture a man who has an electric shock, makes a good recovery and pursues his normal activities including work. Then 10 days later develops an infarction. In the latter case, one would seriously question any relationship between the two events. Electric coma therapy has been used daily for many years by psychiatrists, and there is no evidence in the literature of myocardial infarction occurring as a consequence. A poll of several cardiologists has resulted in the opinion that this phenomenon has not been observed.

Reviews of the case histories of several hundred diabetics do not suggest any exposure to electric shock and it is unlikely that any important relationship exists.

A definitive opinion concerning this case could not be provided without the following information:

I. The Event
   - A. What was the nature of the electric shock?
   - B. What was the immediate clinical course?
   - C. What objective procedures were performed?

II. The Interim
   - A. What was the clinical course during the 10-day interval?

III. The Final Event
   - A. What was the terminal picture from a clinical and laboratory standpoint?

Abstracts of Current Literature

Surgery

Management of Arterial Injuries to Lower Extremity. J. E. Conley* and W. J. Boulanger. Wisconsin M. J. 59-No. 3 185 (March) 1960. (*425 E. Wisconsin Ave., Milwaukee 2, Wis.)

The authors recommend major artery and vein repair in the extremities following trauma. Simple ligation of the common iliac artery results in a 50% incidence of leg amputation; ligation of the femoral results in a 40% loss; and popliteal ligation results in a 60% loss. Hughes had an 11% incidence of amputation following repair of 29 major arterial injuries. With major arterial injuries, associated injuries of nerves, major veins, tendons, and bones are common. Conley and Boulanger outline their concept of therapy. Peripheral pulses are checked and recorded in all extremity injuries. Prompt surgical exploration is done in all cases for injuries at the knee or above without peripheral pulse, with only respiratory impairment or major exsanguination taking precedence. Arteriotomies on all nonpulsating arteries are performed to remove clots. If possible and with defects to 5 cm, end-to-end repair of the artery is preferable to prosthesis. Major veins should also be repaired to prevent residual edema. Anticoagulant therapy is not necessary. Sympathetic blocks prior to surgery waste valuable time and after surgery are of doubtful value. Four illustrative cases are presented. —O.E.M.

Surgical Treatment of Atherosclerotic Occlusive Lesions in Patients with Cerebral Arterial Insufficiency. E. S. Crawford,* M. E. Bakey, W. S. Fields, D. A. Cooley, and G. C. Morris Jr. Circulation 20:168 (Aug.) 1959. (*Cora and Webb Mading Department of Surgery and the Department of Neurology, Baylor University College of Medicine, Houston, Texas)

Realization that extracranial arterial disease is a fairly common cause of cerebral arterial insufficiency led to arteriographic studies in 174 patients with this syndrome. Extracranial arterial occlusion was demonstrated in 73 patients (42%). Where the occlusion involved vessels arising from the aortic arch, clinical diagnosis was frequently possible by the diminution of arterial pulses in the neck or arms, claudication in the arms, and symptoms of cerebral arterial insufficiency (transient paralyses, visual disturbances, dizziness, and headache). The exact localization and extent of the lesions was demonstrated by venous angioaortography by a modified Robb-Steinberg technique utilizing 50 cc of 85% Hypaque solution. Clinical diagnosis of occlusions of the internal carotid and vertebral arteries was not possible. These lesions could be demonstrated only by direct arteriography with 8 cc of 85% Hypaque under local anesthesia.

Surgical treatment was performed in 63 patients with a total of 115 occlusive lesions. Of the lesions 75 were so localized that endarterectomy was possible in 37 instances and the insertion of a flexible knitted Dacron by-pass in the remaining 38. Of the 63 patients, 57 recovered and circulation was restored in one or all of the occluded vessels in 47. All patients with lesions of the great vessels arising from the aortic arch were completely relieved, and the majority of patients with lesions of the internal carotid and vertebral arteries were either relieved or significantly improved. These patients have been followed up to periods of more than five years, and the success achieved by operation has been well maintained. —J.J.T.†

Treatment of an Avulsed Skin Flap Involving the Circumference of the Entire Lower Leg. E. Coryllos,* O. Dahbeck, E. Tracey, and H. Reckman. Ann. Surg. 151:437 (March) 1960. (*Department of Surgery, New York University Post-Graduate Medical School, New York City)

In avulsion type skin injuries the excision of all damaged tissue with immediate application of a full-thickness graft decreases disability and improves final results. If an avulsed flap exists and its length is no longer than its base, it may, after cleansing, be returned to its bed if capillary circulation is satisfactory. This is contraindicated if the flap is longer than its breadth. In this case interception of venous and lymphatic flow causes edema with secondary arterial obstruction, with ultimate tissue necrosis and secondary infection. In these cases the flap should be removed, cleansed, and defatted, and deeply traumatized areas removed. Its site of origin is surgically cleansed and debrided. The skin is then resutured in place as a full-thickness graft, with healing occurring with a high percentage of take in 10 to 14 days. A case is reported in which the skin between the knee and ankle of a 9-year-old was avulsed. It was handled as noted with a take of 80%. The additional areas were treated with split-thickness grafts. —O.E.M.

Severe Crushing Injuries of the Chest: Simple Method of Stabilization. L. H. Strug,* B. Glass, W. Tran, and M. Salatich, J. Thoracic & Cardiovasc. Surg. 39:166 (Feb.) 1960. (*Department of Surgery, Division of Thoracic Surgery, Louisiana State University School of Medicine, New Orleans, La.)

The authors review 154 cases of penetrating trauma of sufficient severity to require hospitalization on the thoracic service during the period 1955-1958. They found 39 cases with flail chest or fractured sternum. Hemothorax, pneumothorax, rupture of the diaphragm, and cardiac injury accompanied many of these. In 15 of the 39, external traction for stabilization was required.

The authors stress the abnormal physiology of

†Listed on editorial masthead page (4a) under "Internal Medicine" abstract category.

a fractured sternum with bilateral costochondral separation. The paradoxical motion must be eliminated if adequate respiration is to be maintained. They stress the practical use of sandbags for positioning of the patient to control paradoxical motion, and condemn adhesive strapping and "rib belts." They describe a useful, simple method of sternal traction by means of sternal screws (Bigelow screws), a bar, and a traction spreader. The screws are inserted under local anesthesia and placed down to the posterior cortex. The bar threaded through the eye of the screws is fixed in place so that good controlled traction can be maintained.

Emphasis is placed on early tracheostomy to reduce the dead space and provide free access to accumulated tracheal secretion. —D.L.

Clinical Orthopaedics—Displacement of Medial Epicondyle into the Elbow Joint. E. Dehne, and C. W. Metz. Clin. Orthopaedics 13:319 (Spring) 1959.

Blount states that in most cases of displacement of a medial epicondyle into the elbow joint open reduction is required. Patrick was able to accomplish reduction of six cases by faradic stimulation of the forearm flexors arising from the epicondyle. Dehne and Metz report that it is possible soon after injury and with a cooperative patient to reduce the displacement when the forearm is stabilized by the operator and the patient is asked to activate the muscles at the elbow. They show x-ray pictures of such a case. They suggest trial of this method prior to open reduction. It should be noted that accurate reduction of this displacement is not essential. If the displacement is not accurately reduced, prominence of the medial epicondyle may occur but there are no growth disturbances. If the lateral condyle is not accurately reduced and properly maintained, definite cubitus valgus will follow.

—O.E.M.

Injuries of the Urinary Tract Due to External Trauma. L. J. Lombardo Jr.,* Arnold M. Heyman, and R. W. Barnes. J.A.M.A. 172:1618 (April 9), 1960. (*1801 Wilshire Blvd. Los Angeles 57)

The authors review the experience at Los Angeles County Hospital over the past five years with external trauma resulting in injury to the penis, bladder, ureter, or kidney. They emphasize that awareness of potential injury should lead to the necessary physical, manipulative, and roentgenologic procedures to clearly establish the integrity of the urinary tract. Further, early diagnosis and effective treatment will produce gratifying results. During this time 13 patients with straddle injuries were seen; of these, 11 were treated without surgery and 1 required perineal repair. All 14 patients with injuries of the pendulous urethra were treated with indwelling catheters. Of 15 patients with posterior urethral injury, 13 required operation. Contusions of the bladder were seen in 16 patients. Rupture occurred in 31, of whom 27 required operation and 4 were moribund. There were five ureteral injuries, all due to gunshot. Of 126 patients with renal injuries, 100 were treated conservatively and surgical intervention was necessary in 24. There was no mortality in the author's handling of these 124 patients. Two patients died preoperatively from other causes.

—N.B.H.

Abstracts

Industrial Hygiene

Air Pollution Hazards from Diesel Locomotive Traffic in a Railway Tunnel. M. Katz,* R. P. Rennie, and Z. Jeghier. A.M.A. Arch. Indust. Health 20:493 (Dec.) 1959. (*Atmospheric Pollution Services, Dept. of National Health & Welfare, Canada, and Research & Development Div., Canadian National Railways)

Plans to substitute Diesels for electric locomotives in a railway tunnel approximately one and one-sixth miles in length prompted this study. The purpose of the survey was to determine the concentrations of smoke, particulate matter, and the principal gaseous contaminants from Diesel trains; to determine the pattern of air flow through the tunnel induced by the train movement; to assess the possible health hazards from tunnel atmosphere; and to evaluate the ventilation requirements to make the environment safe.

The shape, length, location and construction of the tunnel indicated that little, if any, natural ventilation could be anticipated. To conduct the survey stations were set up within, at the ends of, and at a distance from the tunnel. Those within the tunnel served as air-sampling stations; two others controlled train operations; and another served as a medical clinic for taking blood samples. Air movement, barometric pressure, and humidity were measured at the stations on each end. The recreation building at a nearby terminal was used as a chemical laboratory and operational headquarters. More than 2,000 observations were made during three days of Diesel operations on a 24-hour basis.

The methodology of collection is described. Sampling and analytical techniques for the following substances are given: carbon dioxide, carbon monoxide, total oxides of nitrogen, nitrogen dioxide, formaldehyde, sulfur dioxide, oxygen, and smoke. Various tables give data on air contaminants by number of samples, date and time samples were taken, mean and maximum concentrations found. Mean and maximum determinations of carboxyhemoglobin in tunnel personnel before and after exposure to tunnel atmosphere for eight-hour shifts during the three days of testing are shown. Smoking habits of these individuals are shown as "nil," "light," "moderate," and "heavy." The HbCO levels in subjects prior to exposure to the tunnel atmosphere are roughly indicative of smoking habits. After exposure, there was some

bias toward higher HbCO levels in 50% of the 14 subjects, while the remainder showed virtually no change.

Railroad personnel and investigators were checked clinically before, during, and after testing. Aside from three reports of minor eye and throat irritation during heavier-than-usual operations, medical findings were essentially negative both during and after the test period.

The installation of appropriate forced-draft ventilation prior to full-scale conversion of the section from electric to Diesel operation was recommended. "Although average levels of carbon monoxide, carbon dioxide, nitrogen dioxide and sulfur dioxide were well below their respective MAC values (1958), some concern was directed at the concentrations found for total oxides of nitrogen, aldehydes, smoke, and particulate matter." Chemical and physical interaction of these substances were discussed as they related to theoretical possibilities and findings from animal experiments. The displacement and movement of tunnel air produced by trains passing through were also given due consideration in planning for ventilation. —M.K.

Automatic Recording Instruments as Applied to Air Analysis. P. M. Giever* and W. A. Cook. A.M.A. Arch. Indust. Health 21:233 (March) 1960. (*109 South Observatory Avenue, Ann Arbor, Mich.)

This paper updates the development of automatic recording instruments and extends the basic data in this area beyond the date of the publication of the "Encylopedia of Instrumentation for Industrial Hygiene" (1956).

The fundamental principles of design are given for the instruments discussed. The techniques of instrumentation are listed under the areas of electroconductivity, potentiometry, coulometry, amperometry, photometry, ionization, thermal conductivity, and chromotogrpayh. —L.W.S.

The Use of Detectors and Test Kits in Industrial Hygiene Investigation. J. B. Gisclard.* A.M.A. Arch. Indust. Health 21:250 (March) 1960. (*Wright-Patterson Air Force Base, Ohio.)

Properly used, these portable, simple-to-operate kits can become valuable tools in industrial-hygiene investigations. The author describes and illustrates various kits that have been developed recently. It is emphasized that the kits produce meaningful results only if used by personnel trained in the broad areas of industrial hygiene. Values obtained must be integrated with knowledge of operations, work schedules, toxicology, and limitations of the instrument before these values may be translated to management for any needed action. The selection and use of detectors or tests kits should be accompanied by professional appreciation of the entire industrial-health problem involved. —L.W.S.

The British Occupational Hygiene Society's Recommendations Regarding the Establishment of an Occupational Hygiene Service on a National Basis. Ann. Occup. Hyg. 2:85 (Dec.) 1959.

The need for an advisory service in their field has been recognized by the British Occupational Hygiene Society. A working group, consisting of Drs. Norman, Mathew, and Hickish and Mr. Isaacs have considered the problem; Dr. Mathew's memorandum to the Society's Executive Committee is the substance of the Society's views on the subject.

The introduction states briefly that the reasons for the existence of this discipline are better production, better labor relations and improved health. Technical advances in industry necessitate the anticipation of problems and hazards; hence scientific evaluation and control of the working environment are deemed to be as important as the technology of production. The Society believes that the Service should be available to any organization or individual concerned with the working environment, over and above those establishments covered by the Factory Act. The need for such comprehensive coverage is pointed up by the observation that agriculture, the largest industry, and many other types of work, such as office, dock, mining, forestry, transport, and building are not covered by statute to the same extent as are factories. Official agencies should encourage referrals to the Service.

The proposed Service would conduct field work supported by laboratory services and give advice in the following areas: process design, recognition of specific problems, and investigation of hazards; it would issue feasible recommendations, monitor potential hazards, and provide for follow-up monitoring services. The Service should investigate and advise upon the following aspects of occupational hygiene: chemical, dust, comfort conditions, noise, engineering, radioactivity, pathology and biochemistry, clinical and radiological studies, and personal protection. The advisory service would also include an information center, reference library, and a digest of information which would be of value in establishing good public relations as well as supplying information. Research in occupational hygiene would be expected; such research, however, should not take precedence over the actual work of the Service.

Structure and administration of the Service is considered in terms of location of facilities, cooperation with existing organizations, and relationship to government agencies. Financial support of the Service is discussed from three possible bases:

1. Fee for service with charges sufficient to permit financial independence.
2. Nominal fee for service plus public subsidies.
3. Free to all users with complete public support.

The lack of trained people in the field, plus the absence of facilities for training in occupational hygiene, is not known to the public. An embryo service staffed with existing personnel, which

would serve as an example and as an educational body, is suggested as one means of making the public aware of the situation. All relevant disciplines, whose representatives should be of high professional standing, would participate. "Medical advice is essential as it is only a qualified medical practitioner who can in the last resort identify and define harmful factors in the working environment. The engineer, chemist and physicist help in the definition with their specialized techniques and take over completely when it comes to the control of the adverse circumstances."

The report concludes with a short discussion of the need for adequate and judicious public relations. —M.K.

Experimental Toxicology

The Toxicology of the Mono- and Dicyclic Aromatic Hydrocarbons of Industrial Importance: Summary. H. W. Gerarde.* A.M.A. Arch. Indust. Health 21:268 (March) 1960. (*Esso Research and Engineering Company, Linden, N. J.)

The results of a systematic study of the toxicology of the mono- and dicyclic aromatic hydrocarbons and their alkyl derivatives are reported. The monoalkyl derivatives of benzene are metabolized principally by oxidation and degradation of the side-chain to water-soluble urinary metabolites, eliminated as glycine or glucuronic acid conjugates. The polyalkyl derivatives undergo side-chain and ring oxidations, depending on the orientation of the ring substituents. The dicyclic aromatic hydrocarbons increase urinary excretion of ethereal sulfate subsequent to ring hydroxylation. Substitution of the naphthalene nucleus with single small alkyl groups (C_1 and C_2) seems to have much less influence on the metabolic pathway than comparable substitution on the benzene ring. —R.E.E.

Continuous Exposure of Laboratory Animals to Low Concentration of Carbon Monoxide. N. P. Musselman, W. A. Groff, P. O. Yevich, F. T. Wilinski, M. S. Weeks, and F. W. Oberst. Aerospace Med. 30:524 (July) 1959.

Dogs, rabbits, and rats, with matched control groups, were exposed to a concentration of 50 ppm CO continuously for three months, without effect. Neither clinical examinations nor autopsies of animals showed anything significant. —R.E.E.

Toxicological Characteristics of the Gamma Isomer of Hexachlorocyclohexane. E. A. Antonovich.* Pharmacol. J. Toxicol. (USSR) 22:275 (May-June) 1959. (*Ukranian Research Institute of Nutrition)

The minimum toxic, minimum lethal, and LD_{100} values of the highly toxic gamma isomer of hexachlorocyclohexane are given for mice and rats. Similar data are presented on the results of chronic exposures of cats for 9 to 12 months. The compound appears to have a neurotropic effect. After repeated dosing, leukocytosis and a reduction in Hb level were seen, also changes in the immunobiological (phagocytic) reactivity, and disturbances in glycogen formation and kidney function (albuminuria). Less cumulative toxicity was seen with the gamma isomer than with DDT and "Hexachlorane." —R.E.E.

Absorption of Methyl ω-(Trimethylsilyl) Dodecanoate and Trimethylhexadecylsilane from the Gastrointestinal Tract of Rats. J. Paul* and W. F. R. Pover. Arch. Biochem. & Biophysics 87:312 (April) 1960. (*University, Birmingham, England)

Two oil-soluble organosilicon compounds, methyl ω-(trimethylsilyl) dodecanoate and trimethylhexadecylsilane, each containing one silicon atom, were dissolved in olive oil and fed to rats at a level of 3% of the diet for five to eight days to determine absorption from the gastrointestinal tract. The former was about 50% absorbed, and the latter only 37%. No significant amount of either compound was absorbed via the lymphatic pathway. Only a small amount of organosilicon material was extractable from the liver lipids, and a small amount of soluble silica was detectable in the urine. It is suggested that, after reaching the liver via the portal circulation, most of the material absorbed is metabolized and is present in the blood, liver, spleen, kidneys, and carcass as soluble silicates in combination with tissue components. Investigations to confirm this are in progress. —R.E.E.

The Metabolism of 1,2-Benzanthracene in the Rabbit. K. H. Harper. Brit. J. Cancer 13:746 (Dec.) 1959.

The hydroxylation of 1,2-benzanthracene in the 2'-position and the lack of carcinogenicity in the rabbit is consistent with the theory that an ortho form of binding is favored during hydroxylation in the microsomes of this species. Its carcinogenic action in the mouse is then envisaged as a secondary effect arising from an initial "poisoning" of the defensive orthomechanism, which then allows the active paraform to come into play. Similar considerations may also apply in the case of 1,2,5,6,-dibenzanthracene (inactive in the rabbit) and 3,4-benzpyrene (reduced activity in the rabbit). —R.E.E.

Toxicology of Isomers of Hexachlorocyclohexane. E. N. Burkatskaya.* Pharmacol. & Toxicol. (USSR) 22:273 (May-June) 1959. (*Kiev Institute of Industrial Hygiene and Occupational Diseases)

A comparative study of the toxicity of the alpha, beta, and gamma isomers of hexachlorocyclohexane revealed the gamma isomer to be the most toxic for mice, rats, cats, and rabbits. Dose-response data are given. Acute intoxication suggested central nervous system disease, and the compound appears to have some cumulative toxic properties. Chronic poisoning produced blood changes characterized by acceleration of erythrocyte sedimentation, leukocytosis, neutrophil shift to the left, and reduction of number of erythrocytes. All isomers

are slightly irritating to the skin of rabbits; the gamma isomer was toxic by skin absorption. Morphological changes produced by the isomers in acute poisoning consisted in venous congestion of internal organs and the brain; after repeated exposures there were internal organ congestion; cloudy swelling of myocardium, kidneys and liver; fatty degeneration of the liver; and dystrophic changes in nerve cells of the brain. —R.E.E.

Isolation of Triethyllead Ion from Liver After Inhalation of Tetraethyllead. C. D. Stevens,* C. J. Feldhake, and R. A. Kehoe. J. Pharmacol. & Exper. Therap. 128:90 (Jan.) 1960. (*Kettering Laboratory, University of Cincinnati, Cincinnati, Ohio.)

Triethyllead (TEL) ion, isolated as the benzoate salt, was detected in liver tissue of rats exposed to (TEL) vapor. Details of the two analytical techniques used are given. These results suggest that therapy of TEL poisoning should take into account the presence of triethyllead ion, a monovalent electrolyte that probably cannot be chelated but which does react with thiol and other groups. —R.E.E.

Absorption and Distribution of $S^{35}O_2$ Inhaled Through the Nose and Mouth by Dogs. O. J. Balchum,* J. Dybicki, and G. R. Meneely. Am. J. Physiol. 197:1317 (Dec.) 1959. (*Vanderbilt University Medical School and Hospital, Nashville, Tenn.)

Dogs breathing $S^{35}O_2$ through the nose and mouth retained a smaller proportion of the inhaled gas in the trachea, lungs, hilar lymph nodes, liver, and spleen than those breathing similar concentrations via a tracheostomy. This conclusion is substantiated by tissue S^{35} concentration assays and measurements of the compliance of the lungs and thorax and of pulmonary resistance. The upper airways, therefore, partially protect the lungs from exposure to SO_2. (Authors' abstract.) —R.E.E.

Inhalation Toxicity of Cobalt Hydrocarbonyl. E. D. Palmes,* N. Nelson, S. Laskin, and M. Kuschner. Am. Indus. Hyg. A. J. 20:453 (Dec.) 1959. (*New York University, Institute of Industrial Medicine, New York.)

Cobalt carbonyl is about half as acutely toxic as nickel carbonyl via the inhalation route, based on a 30-minute LC_{50} of 165 mg Co/cu m for the rat. The response was typical of a strong pulmonary irritant, but the evidence of lung edema and pneumonia, present in those animals killed 24 hours after exposure, had disappeared in those surviving 2 weeks after exposure. Rats, guinea pigs, and dogs exposed over a period of three months to 9 mg Co/cu m (71 six-hour exposures) appeared to be in good health at the end of the exposure. A rapid turnover of the bulk of inhaled material was observed in that a substantial fraction appeared in the urine within one day after exposure; urinary levels dropped by about one-half for each day after removal from exposure. The definite and persistent elevation in rat hemoglobin values observed was interpreted as a physiological change due to cobalt. The significance of foam-cell aggregates seen in the lungs of repeatedly exposed dogs is not known; these disappeared after exposure was stopped. An eosinophilic pneumonia seen in one guinea pig given a single additional exposure, six months after stopping the repeated exposures, was interpreted as suggestive of an allergic response. Cobalt carbonyl broke down rapidly in air to uncharacterized inorganic cobalt compounds. Methods of measurement, sampling, and analysis are included. —R.E.E.

Mental Health

Psychiatric Consideration in Whiplash Injuries of the Neck. R. L. Leopold* and H. Dillon. Pennsylvania M. J. 63:385 (March) 1960. (*Department of Neurology and Psychiatry, Graduate School of Medicine, University of Pennsylvania, Philadelphia.)

This article is based upon an analysis of 47 cases of whiplash injury observed in 1958 and 1959. There is very little literature relating to the emotional factors in this type of injury. Evaluation is difficult because there often is cerebral concussion. Most of these injuries are a result of automobile accidents.

Patients with emotional components usually have delayed recovery and exhibit anxiety, apprehension, and tension. Factors which may lead to the development of this type of emotional complication include tedious investigation, litigation worries, and concern about compensation. This type of patient initially does not feel the full extent of the injury—after a superficial examination, he is told that there is not very much wrong with him, but the patient becomes increasingly anxious, and neuromuscular tension may add to his pain. Meanwhile, he becomes angry with the person who has caused the accident and returns to his physician from time to time attempting to justify his complaints.

The authors were struck by the number of eye complaints. They attribute these to brain-stem involvement even in cases where there is no unconsciousness. There is no relationship between the severity of the injury and the emotional reaction, for the most severely injured patients had the least severe emotional reactions both subjectively and objectively.

The authors discuss typical cases and suggest that the suddenness of the accident and injury prevents the person from preparing for the unpleasant experience. Sometimes a defense mechanism of denial may be involved. They feel that the fact that the head and neck are involved adds to the problem—the head symbolizing control of behavior. The emotional reaction is not significantly related to preexisting psychological disease, as is sometimes contended. —G.C.T.

Abstracts

Diagnosis of Intermediate Stage of Alcoholic Brain Disease. A. E. Bennett.* J.A.M.A. 172:1143 (March 12) 1960. (*Herrick Memorial Hospital, Berkeley, Calif.)

Alcoholic brain disease heretofore has been classified as either an acute state or a chronic brain syndrome, the latter involving cortical atrophy and midbrain changes. The author contends on the basis of his observations that a large number of alcoholics actually are in a middle zone, and this he terms the intermediate brain syndrome. There is an increase in the incidence of alcoholic brain damage in the United States—about 20% of admissions to state hospitals are now for alcoholism. In his study of the electroencephalograms of 758 alcoholic patients admitted to the psychiatric department of a private general hospital, at least one-third had abnormal EEG's The patients in this intermediate stage of alcoholism have personality changes including "rationalization of drinking, pathological lying, infantile behavior, poor judgment, hostility, emotional lability, and lack of insight." It is stated that there are delirious or convulsive episodes in about 50% of cases—a higher figure than one would have expected. Bennett also believes that the symptoms are not those of a neurotic personality but are due to organic brain damage, resembling the frontal lobe syndrome. On psychological testing, there is evidence of impaired power of abstraction and intellectual deterioration. It is very important to recognize this stage in the alcoholic. The patient must, of course, abstain from alcohol absolutely, and in 50% of cases other systemic diseases such as liver damage must be treated for some time. Patients may require hospitalization or close supervision at home until insight is possible, at which time psychotherapy and Alcoholics Anonymous are of help in maintaining rehabilitation. —G.C.T.

Modern Human Relations in Perspective. W. G. Scott.* Personnel Admin. 9:2 (Nov.-Dec.) 1959. (*Associate Professor of Management, College of Commerce, De Paul University, 64 East Lake St., Chicago.)

The general assumption is made that human relations involves several disciplines but that it is greater than the sum of the disciplines of which it is composed. This provides an understanding of people which qualifies human relations to solve problems of human conflict more adequately.

A number of action-designed assumptions are presented. These are needed so that management can establish the philosophy from which policies and procedures may be evolved: (1) The key is that good human-relations practice is the product of the manager using experience, intuition, and interdisciplinary generalizations to guide him. (2) Employee participation is essential to higher productivity and to morale. (3) The assumption of role is the set of expectations confronting the person at work. These are the job-oriented role and the informal-group-oriented role. (4) The assumption of communication—referred to as the "nervous system of the organization"—is that of "good communication," and it is conceded that this is not entirely within the area of human relations. It may be partly an engineering matter, but nevertheless it is of great importance. (5) Teamwork is an essential element of management practice. (6) Man is diversely motivated with a hierarchy of needs which is changeable. (7) The plant is a social system. (8) Executive skills in human-relations practice can be developed.

Two general criticisms of human relations labelled "introversion" and "shortsightedness" are outlined. By introversion is meant exclusively concentrating upon the internal structure of the plant or on the industrial problem without considering the larger context and the larger institutional setting. This has been expressed as a human relations' "tight little island" . . . vision. The shortsightedness criticism is that human relations does not focus sufficiently upon the work activity but puts too much emphasis upon interpersonal relations and upon the group and overlooks the analysis of the worker and work. Modern human relations tend to neglect the economic dimension of work satisfaction. Studies indicate that the economic incentive is by no means first on the list of the employee's needs. The author points out that "this is much like saying, man does not live by bread alone, once he has bread."

The article concludes with the unanswered question of whether management is responsible for the full development of the employee. —G.C.T.

The Trauma in "Traumatic Neurosis." H. C. Modlin.* Bull. Menninger Clin. 24:No.2 (March) 1960. (*Menninger Foundation, Topeka, Kan.)

During the past five years, the number of patients referred to the Menninger Clinic with a presumptive diagnosis of "traumatic neurosis" has shown a steady annual rise. This paper discusses some aspects of the illness in 40 such patients. Its discussion is confined to a clinical analysis of the psychological stress factor in the traumatic-neurosis syndrome frequently seen following accidents.

Two sets of circumstances are identified in this paper as operative in initiating the syndrome. In the first, the patient-to-be experiences a brief forewarning of an impending disaster. In the second set of circumstances, the accident occurs suddenly, unexpectedly, without forewarning. Two examples of cases with each set of precipitating circumstances are cited.

Dr. Modlin includes the following symptoms in the syndrome: anxiety; chronic muscular tension; repetitive frightening dreams; irritability; and withdrawal—most commonly expressed in loss of sexual interest, poor concentration and memory, avoidance of social contacts, and intolerance of discussing symptoms or the traumatic event.

ABSTRACTERS NOTE: The study suggests that the syndrome may be a fundamental, nonspecific reac-

tion to severe external stress. If this is the case, the importance of early recognition should become a paramount concern for the occupational physician. Complementary comment to this point may be found in Ross's discussion of "Accidents and Their Sequelae."

This paper and subsequent reports of similar research should be read in their entirety by physicians interested in the increasing problem of compensation for the psychiatric sequelae of accidental injury as well as for greater understanding of common psychological factors operative in such cases.

—A.A.M.

Dermatology

Anaphylactoid Reactions to Oral Administration of Penicillin. J. M. Batson.* New England J. Med. 262:590 (March 24) 1960. (*Department of Medicine, New York Hospital, New York.)

Reactions to Penicillin may be of the immediate, accelerated, or delayed type. Only the immediate type associated with severe systemic reactions such as hypotension and often a shocklike state should be referred to as "anaphylactoid."

Welch and co-workers in a survey of more than 800 hospitals and 1,600 physicians during the period of late 1953 to early 1957 found 611 anaphylactoid reactions to intramuscular penicillin with 63 deaths. Parenteral administration of penicillin and streptomycin combinations produced 122 reactions with nine deaths. Penicillin by mouth produced 49 anaphylactoid reactions without a single death.

Although the oral route for administering penicillin appears much safer, it is not entirely without dangers. Batson reviews 26 cases, 2 of which ended fatally. Clinical data of these reported cases of anaphylactoid reactions to oral penicillin are carefully tabulated and summarized. Two additional nonfatal cases of anaphylactoid reactions are presented. —W.R.B.

Dermatitic and Pigmentary Reactions to Monobenzyl Ether of Hydroquinone. C. S. Dorsey.* A.M.A. Arch. Dermat. & Syph. 81:245 (Feb.) 1960. (*Department of Dermatology, University of Southern California School of Medicine, Los Angeles.)

Leukoderma occurring in human skin after external contact with the monobenzyl ether of hydroquinone was first brought to the attention of dermatologists by Oliver and others in 1940. Studies over the past 5 years of its use in ointment form have revealed that some 13% of persons so treated develop a contact dermatitis to the material. Some of these persons, probably fewer than 1%, develop hyperpigmentation or leukodermic skin changes.

The author reports two cases in which ointments containing monobenzyl ether of hydroquinone were used. Normal pigmentation has not returned in either patient over an approximate three-year followup period of time. Rather the pigment return has been only some 20% to 40%. —W.R.B.

Basal Cell Cancer in Children and Young Adults. J. E. Murray* and B. Cannon. New England J. Med. 262:440 (March 3) 1960. (*Harvard Medical School, Boston, Mass.)

Forty-one cases of basal-cell carcinoma occurring in 27 male and 14 female patients under age 30 were studied by the authors. Nine of the patients gave no history of a preexisting lesion. Fourteen of the patients had a diagnosis of mole, hemangioma, or papilloma as the preexisting lesion which appeared to be activated by slight trauma and failed to heal spontaneously. Six of the patients had preexisting scars subsequent to hot-metal burns, and two followed excessive exposure to irradiation or sunlight. Four other cases followed, respectively, a simple forehead laceration, a metallic foreign body, a bayonet injury, and electrodessication. —W.R.B.

An Epidemic of Coccidioidomycosis Probably Related to Soil. B. Joffe.* New England J. Med. 262:720 (April 7) 1960. (*Cardiopulmonary Laboratory, Mount Zion Hospital, San Francisco, Calif.)

The author discusses an outbreak of coccidioidomycosis that occurred after excavation of tracts of land of considerable size for dwelling units. The tracts were located at Edwards Air Force Base in Kern County, Calif.—some 100 miles northeast of Los Angeles and at the edge of the Mojave Desert. Excavation was carried out by bulldozers to a depth of some 15 cm, and no attempt was made to thoroughly wet the scraped dirt. The powdered dirt was blown by prevailing winds over the remainder of the base. A field test, made prior to the excavation, to determine the airborne fungus population revealed no spores of Coccidioides immitis, and a low average fungus population. This finding points out the importance of examining soil to the depth of the intended excavation when looking for viable spores of C. immitis rather than being content with surface soil or airborne fungus examinations alone. In all, some 33 cases of coccidioidomycosis occurred at the air force base. In 3 of the cases there was serologically proved active infection without any symptoms—the only positive finding being a skin rash. This paper is the first to report such a manifestation. Coccidioidomycosis is a dustborne disease. Endemic areas requiring soil excavation should be oiled and wetted and subsequently grassed. —W.R.B.

Penetration of Anionic Surfactants (Surface Active Agents) into Skin. I. H. Blank* and E. Gould. J. Invest. Dermat. 33:327 (Dec.) 1959. (Department of Dermatology, Massachusetts General Hospital, Boston 14.)

Data are presented on the penetration from aqueous solutions of sodium laurate, a constitu-

ent of most soaps, into excised human skin. Similar data are presented for the sodium salt of dodecyl sulfate, a representative alkyl sulfate and a constituent of the earlier synthetic detergents used in the household. It was shown that both salts penetrated the stratum corneum. Relatively little sodium dodecyl sulfate reached the epidermis below the major barrier of the skin, however. This finding was noted when using weak, unbuffered, mildly alkaline solutions. When the salt solutions were alkaline to a greater degree (greater than 10.5), both surfactants penetrated into the dermis through the alkali-damaged barrier of the skin. —W.R.B.

Internal Medicine

Diabetic Diarrhea with Malabsorption Syndrome. M. Ellenberg* and J. J. Bookman. Diabetes 9:14 (Jan.-Feb.) 1960. (*Department of Medicine and Metabolic Clinic, Mt. Sinai Hospital, New York.)

Two female patients in their fifth decade with diabetes for the preceding 30 to 35 years developed the "sprue syndrome" along with evidences of malabsorption. Vitamin B_{12} was ineffective in both cases. The addition of folic acid and liver extract was without effect in one of the two. Both responded promptly and dramatically to corticosteroid therapy. The authors believed the syndrone to be "conditioned" by the prolonged diabetic state. —L.W.

Retinopathy and Nephropathy in Diabetes Mellitus. S. Johnson.* Diabetes 9:1 (Jan.-Feb.) 1960. (*Department of Medicine, University of Lund, General Hospital, Malmö, Sweden)

Late in the 1930's, relaxation of previous rigid dietary controls became failry common in the treatment of diabetes mellitus in many clinics. Moderate glycosuria and hyperglycemia were often tolerated so long as ketonuria or polyuria did not occur. The author attempts to compare the incidence of retinopathy and nephropathy in a selected group of diabetics treated in this manner with the incidence in a similar group treated according to earlier, more rigid standards.

All diabetics in the relatively small city of Malmö, Sweden, has been cared for at the same hospital, where uniform methods of therapy were instituted at the onset of the disease. Those discovered between 1922 and 1935 are compared with those discovered between 1936 and 1945. The number of surviving members of the latter group is about twice that of the earlier group. The age of onset was almost the same in the two groups (average 20.9 and 19.3 years). Obviously, the earlied group has been followed longer than the other (average 24.5 and 15.9 years). Nephropathy, as evidenced by proteinuria, was detected, however, in only 32% of the earlier group as compared with 54% of the latter. If only those with diabetes of 15 or more years' duration are compared for proteinuria at the end of 15 years' observation, the difference is even more striking —9% and 61%. Similarly, the severity, but not the frequency, of retinopathy was notably greater in the more recent group, even though the average duration of the diabetes was 10 years' less. Frequent insulin coma did not favor the appearance of retinopathy or nephropathy. —L.W.

Use of a New Vasodilator Agent in Management of Peripheral Arterial Insufficiency. S. S. Samuels* and H. E. Shaftel. J.A.M.A. 171:142 (Sept. 12) 1959. (*151 E. 83rd Street, New York.)

The present study of 46 patients was undertaken to determine the effectiveness of a new vasodilator, isoxsuprine (Vasodilan), in peripheral artery insufficiency. Subjectine improvement such as decreased sensations of cold and relief of pain or cramps was not considered; the focus of attention was an objective improvement during isoxsuprine therapy.

Objective improvement was indicated by increased walking capacity in blocks and improvement in digital blood flow as measured by plethysmography and oscillometry. Walking capacity was increased in 86% of the patients. The mean walking capacity before treatment was 3.2 blocks and after treatment 7.8 blocks. Digital blood flow to the finger after isoxsuprine increased about 50%, and the blood flow to the toe increased about 97%.

Three patients had gangrene of the lower extremity. Complete healing occurred in two, and the third was healing satisfactorily at the time of the report. Two patients were diabetic. Isoxsuprine had no effect on the blood-sugar level or on insulin or tolbutamide requirements. Isoxsuprine apparently does not increase the caliber of normal vessels and rob the blood supply to ischemic tissue as has been claimed with other vasodilators (the borrowing and lending phenomenon).

It is concluded that isoxsuprine is effective without significant side effects, and no phenomenon occurred to suggest any contraindications. It seems well suited for office management of patients with peripheral vascular disease. —S.H.S.

Phenethylbiguanide, a New Orally Given Hypoglycemic Agent: Report After Two Years of Clinical Experience. J. Pomeranze,* G. T. Mouratoff, R. J. Gadek, and E. J. King. J.A.M.A. 171:252 (Sept. 19) 1959. (*Fifth Avenue, New York.)

The present study was undertaken to determine the efficacy of phenethylbiguanide (DBI) as a hypoglycemic agent. The report is based on a two-year study of 206 diabetic patients treated with DBI alone or in combination with insulin. It was demonstrated that DBI reduces blood-sugar levels within three hours after oral administration of glucose in both severe and mild cases of diabetes mellitus. The definite mode of action of DBI remains uncertain, but it may specifically influence the metabolic lesion of diabetes because it has no

effect on the blood-sugar levels of nondiabetic persons.

The standards of good control are consistently negative 24-hour urine specimens and a two-hour postprandial blood-sugar level of not more than 200 mg% or a fasting blood sugar of less than 150 mg%. The authors conclude that DBI is a useful hypoglycemic agent. Insulin therapy may be discontinued in a significant percentage of diabetics. It may be used with insulin for better control in severe diabetics. The present age of the patient, the age at diagnosis, the known duration of diabetes, and the duration of insulin therapy do not determine the effectiveness of DBI. No organ toxicity was observed, and the only side effects were gastrointestinal, which necessitated the withdrawal of therapy in 26% of the patients treated. —S.H.S.

Potassium-Secreting Tumors of the Large Intestine. A. D. Roy* and H. Ellis. Lancet 1:759 (April 11) 1959. (*Consultant Surgeon, Western Infirmary, Glasgow, Scotland.)

Villose tumors of the large intestine associated with hypopotassemia were first described in 1956. Seven cases have so far been reported, including the two described in this paper. It may be that such cases are not rare but are unrecognized.

The authors describe two cases of circulatory collapse due to dehydration and hypopotassemia occurring in individuals with villose tumors of the colon. Both patients were seriously ill; they were in circulatory collapse and markedly dehydrated. Each gave a history of loose stools, often watery with mucus but never blood-stained. It is suggested that the volume of fluid lost is directly related to the surface area and size of the tumor, and it also is suggested there may be active secretion of potassium by the tumor cells, or the fluid secreted by the tumor may be isotonic with plasma, and therefore there is reabsorption by the epithelium of the colon. The potassium concentration of the rectal fluid was 3½ to 16 times that of the plasma.

It is concluded that villose tumors of the colon and rectum are not rare. Physicians should consider such a diagnosis in patients with a history of watery stools without blood, and who may be first seen as an emergency patient in circulatory collapse. —S.H.S.

Atypical Face Pain. J. G. Rushton,* J. A. Gibilisco, and N. P. Goldstein. J.A.M.A. 171:545 (Oct. 3) 1959. (*Mayo Clinic and Mayo Foundation, Rochester, Minn.)

The authors examined 100 patients who complained of "atypical face pain" which the authors classified as pain which did not refer to trigeminal neuralgia, glossopharyngeal neuralgia, postherpetic neuralgia, or pain secondary to disease of teeth, throat, nose, sinuses, eyes, or ears. It is deep, poorly localized, unanatomic in distribution, constant, of long duration (weeks or years), and lacks trigger zones.

The condition was classified in three categories: (1) psychogenic, (2) organic, and (3) indeterminate. The group classified as psychogenic exhibited positive evidence of psychiatric illness. Organic face pain was due to (*a*) vasodilatation, (*b*) dental disease, (*c*) neuritis, the presumed cause being trauma, (*d*) neoplasms of the parotid and antrum and a neurofibroma of the acoustic nerve, and (*e*) miscellaneous. Thyroiditis was included in this group, as was temporal arteritis. In the indeterminate group, no definite cause could be found to account for the face pain. In more than 50% of the 14 cases in this group, the onset of pain was after 50 years of age and the duration was relatively short.

The authors caution that "atypical face pain" should not be considered an entity, as this implies a common cause and a definite diagnosis. Patients complaining of face pain deserve a careful physical examination. Many will require x-ray examination of the skull, sinuses, teeth, cervical spine, and temporomandibular joints. The term atypical face pain should be used only after exhaustive study has failed to reveal a definite cause. —S.H.S.

Hypoglycemic Insulin Reactions Without Warning Symptoms. M. C. Balodemos* and H. F. Root. J.A.M.A. 171:261 (Sept. 19) 1959. (*15 Joslin Road, Boston, Mass.)

Recently 116 diabetics have been studied who developed hypoglycemia without the usual prodromal warning signs, such as hunger, tremor, sweating, and diplopia. While awake, these patients lapse into stupor or unconsciousness with or without convulsions. The blood-sugar level drops quickly and confusion and unconsciousness occurs without symptoms. The majority had had diabetes for a long time and knew the usual early warnings of hypoglycemia through experience. Many in this group were unstable diabetics—minor variations in insulin dosage, diet, exercise, or combination thereof causing insulin reactions.

The central nervous system apparently undergoes some changes so that its response to insulin-induced hypoglycemia is altered. It may be a cerebral metabolic change so that the usual early responses are annihilated, it may be cerebral vascular, or there may be a diabetic neuropathy of the autonomic nervous system. Finally, epileptic equivalents must be considered. Organic lesions causing spontaneous hypoglycemia by increased insulin production should also be considered. Among these are adenoma and carcinoma of the pancreas and lesions of the hypothalamus. Anterior pituitary and adrenocortical hypofunction and hepatic diseases should also be considered.

The authors conclude that to prevent these serious reactions insulin dosage must be regulated carefully: long-acting insulin early in the day and short-acting later doses and strict dietary control with frequent inbetween feedings. —S.H.S.

Prophylaxis of Ischaemic Heart Disease by Thyroid Therapy. B. O. Barnes.* Lancet 2:149 (Aug. 22) 1959. (*1160 S. Colorado Blvd., Denver, Colo.)

There apparently is a relationship between hypercholesteremia and myocardial infarction. There is also apparently some correlation between hypercholesteremia and thyroid activity.

The present study was undertaken to determine whether subnormal thyroid function existed in a greater number of patients with hypercholesteremia than heretofore supposed. The author's study indicates that such is the case. The investigation was extended to determine if (1) thyroid therapy would control hypercholesteremia before evidence of arteriosclerosis was detectable, (2) thyroid therapy would benefit patients who already had suffered myocardial infarction, (3) the incidence of arteriosclerosis could be reduced by long-term therapy. The discussion indicates that thyroid therapy will reduce hypercholesteremia.

It will restore the circulation time to normal in myxedema, in which condition it is prolonged, and apparently it will increase coronary blood flow in cases of myocardial infarction.

Eighty cases of hypercholesteremia in apparently normal adults were investigated. In all cases, evidence could be found in the history or physical examination or in laboratory data of subnormal thyroid function. Thyroid therapy reduced average blood cholesterol levels. Four patients with myocardial infarction were treated with thyroid and clinical improvement noted. The author points out that heart damage recently reported during thyroid therapy occurs when overdosage is used. —S.H.S.

Radiation Health

Radiation Health Problems As They Relate to Epidemiology. C. L. Dunham.* Am. J. Pub. Health 49:1607 (Dec.) 1959. (*Division of Biology and Medicine, Atomic Energy Commission, Washington, D. C.)

Where exposure to either internal or external radiation has been gross, the cause and effect relationship is established with relative ease. Radiation burns, skin cancer in radiologists, and osteitis, bone sarcoma, and anemia in radium dial painters exemplify such cause and effect relations. Since the advent of nuclear fission and increased potential for exposure of individuals and populations to increasing amounts of radiation, epidemiological research in this field has expanded rapidly.

While an increased incidence of leukemia has been demonstrated in radiologists, studies have failed to show life shortening among this group. Other studies have shown many cause and effect relationships between fairly large acute or chronic exposures and radiation cataracts, leukemia, cancer, etc. The demonstration of cause and effect relationship in the case of chronic low-level exposure is a very difficult problem, calling for the use of the "most sophisticated of modern epidemiological methods." Such studies "will require extremely careful advance planning because of the welter of biological and environmental factors whose action can be confused and compounded with any action that might be produced by the radiation exposure." —W.D.N.

Acute Radiation Sickness and Its Delayed Consequences. Abstracts of Reports and Information on the Conference of October 19 to 21, 1959. Edited by B. A. Lapin. U. S. Atomic Energy Commission, Technical Information Service Report AEC-tr-3924. (Available from the Office of Technical Services, Department of Commerce, Washington 25, D. C., $1.25.)

Translated abstracts of some 20 papers of the conference at the Institute of Experimental Pathology and Therapy of the Academy of Medical Science of the USSR, Sukhumi, are compiled. Evident is considerable work on the clinical, biochemical, neurological, morphological, and functional changes brought about by radiation (generally acute) in mice, rats, guinea pigs, rabbits, cats, dogs, monkeys, and humans. Some papers were on the prophylactic effects of several compounds, and one concerned treatment. One paper covered work on 40,000 mice, 2,000 rats, guinea pigs, and cats, and 150 monkeys. One paper reported on the use of transitional epithelium (bladder) transplanted subcutaneously in guinea pigs to maintain extramedullary formation of myeloid tissue. —T.S.E.

Congress Acts to Give States Radiation Control Authority: HEW's Role Increased. Science 130: 779 (Sept. 25) 1959.

Legislation passed in the closing days of Congress establishes a permanent National Radiation Council to advise the President on radiation matters. "It authorizes the AEC to withdraw its control over certain materials, principally radioisotopes, but not over more hazardous activities, such as the licensing and regulation of reactors. It requires that federal and state radiation standards be compatible and authorizes programs to assist the states to assume independent regulatory jurisdiction." This legislation does not substantially alter the roles of AEC (Atomic Energy Commission) and HEW (Department of Health, Education, and Welfare) in the areas of radiation-health control, although, through its membership in the President's radiation council, HEW will now play an active part in the formulation of standards and policies and in the coordination of responsibilities at the federal and state level. Further, the President has issued a directive that HEW, in order to advise him and the general public, should intensify its radiological-health effort and have primary responsibility within the executive branch for the collection, analysis, and interpretation of data on environmental-radiation levels, such as fallout. —W.D.N.

Abstracts

X-ray Emission from Television Sets. C. B. Braestrup* and R. T. Mooney. Science 130:1071 (Oct. 23) 1959. (*Physics Laboratory, Francis Delafield Hospital, New York.)

Electronic tubes operating at a potential of above a few thousand volts may be a source of x-radiation. This study includes an estimate of the average per capita dose to the gonads from home television sets, based on radiation measurements from representative types of television tubes and the results of laboratory depth-dose measurements required to determine the actual dose to the gonads. International Commission on Radiological Protection recommended that the emission of x-rays should not exceed 2.1 mr per hour at any accessible surface on home television sets. Consideration has since been given to lowering this value to 0.5 mr per hour at 5 cm from any accessible surface of the set. Using this latter figure, viewers at 200 cm receive an estimated yearly average gonad dose of less than 5 mrad. This may be compared with the gonad dose due to natural background, which is of the order of 100 mrad per year. —W.D.N.

The Brookhaven Medical Research Reactor. L. E. Farr.* Science 130:1067 (Oct. 23) 1959. (*Brookhaven National Laboratory, Upton, New York.)

This is the only nuclear reactor conceived, designed, and built solely to add knowledge of certain aspects of medicine. The reactor provides two shielded rooms, on either side of the reactor, primarily to further studies on neutron effects with particular reference to development of neutron capture therapy. Vertically moving shutters weighing 20 tons are used to control neutron and other radiation emission through special ports into these rooms. By appropriate selection of moderating liquid, screen, filter, and shields, a variety of effects can be obtained. The reactor will permit not only exploration of the practical application of neutron-capture therapy but also will make intricate studies of the mechanism of energy transfer to biological systems from neutrons of epithermal and intermediate energy. —W.D.N.

The Role of X-Ray Therapy to the Neck Region in the Production of Thyroid Cancer in Young People. A Report of 37 Cases. E. H. Wilson* and S. P. Asper, Jr. A.M.A. Arch. Int. Med. 105:244 (Feb.) 1960. (*601 North Broadway, Baltimore, Md.)

A study of 37 patients with histologically proven cancers of the thyroid at or under the age of 25 is presented. Sixteen (43%) had previously received radiation therapy to the head, neck, or chest for thymic enlargement, acne, chronic tonsillitis, hemangioma, enlarged tongue, and laryngeal polyps.

In those operated for cancer of the thyroid at 17 years of age or younger, 13 (72%) had previously received therapeutic radiation, whereas in the group operated at ages ranging from 18 to 25 only 3 (16%) had previously received such radiation therapy. These data indicate a significant incidence of preceding radiation in children with thyroid cancer and support the concept that x-ray therapy is a factor in the development of thyroid cancer in young persons. —W.D.N.

Environmental Physiology

Effects of High and Low Humidity on Heat Exchange of Lightly Clothed Men. P. F. Iampietro* and E. R. Buskirk. J. Applied Physiol. 15:212, 1960. (*Quartermaster Research and Engineering Center, Natick, Mass.)

Although it is common experience that the sensation of chill seems greater on cold humid days than on days when the air is dry, previous studies on nude subjects conducted by these and other investigators failed to demonstrate a significant difference in body heat loss to cold humid air compared with dry air at the same temperature. To test the hypothesis that humidity may exert its effect by altering heat exchange through clothing, the present study repeated the earlier tests using six male subjects dressed in cotton garments consisting of socks, underwear, shirt, and trousers, together with low shoes. The resting subjects were exposed for two hours at different combinations of air temperatures (50° and 40°F), humidities (100% and 30%), and air movements (10 and < 1 mph). Rectal temperature, skin temperature, and metabolic rate measured during exposure revealed significant differences in heat loss and heat production related to air temperature and air movement but no influence of humidity on heat exchange could be detected. The authors suggest that the increased sensation of chill on cold, wet days may be related to other climatic factors such as overcast with reduced solar radiation or to alterations in heat balance associated with changes in activity. —D.M.

Is Humidity Important in the Temperature Comfort Range? Walter Koch,* B. H. Jennings, and C. M. Humphreys. J. Am. Soc. Heating, Refrigerating, and Air-Conditioning Engineers 2:63 (April) 1960. (*ASHRAE Research Laboratory, Cleveland, Ohio)

Since 1923 engineers have used the Effective Temperature (E.T.) Scale of Houghten and Yaglou as a guide in designing air-conditioning systems for human comfort. All combinations of air temperature, humidity, and air movement which produce an immediate thermal sensation equivalent to that of a reference environment in which the air is 100% saturated and without movement are said to have the same E.T., which is defined as the air temperature of the reference environment.

In general the lower the humidity the higher is the air temperature required to give the same E.T. For some years, however, there have been indications that the normal scale of E.T. overemphasizes the role of humidity in the comfort

zone. This paper provides experimental support for this view.

Groups of young adult male and female subjects sitting quietly in light clothing were exposed for periods of three and one-fourth hours to different combinations of dry and wet bulb temperature at air movements less than 20 fpm. Each half-hour, subjective reactions to the thermal environment were recorded on a 7-point scale, 4 representing comfort. Attainment of thermal equilibrium required up to three hours. Plotted on linear coordinates of dry and wet bulb temperature, the regression line for group mean scores for optimum comfort was a straight line extending from 77.6°F dry bulb at 30% RH to 76.5°F at 85% RH. By contrast, the E.T. line for 71° requires a change of 7.7° dry bulb for the same humidity range. The larger influence of humidity on the immediate sensory response on which the E.T. scale is based is believed to result from humidity effects on heat absorption or loss from clothing fabrics. These effects are transient and disappear during prolonged exposure.

For most purposes, therefore, dry bulb temperature alone is the best guide for predicting subjective responses in the comfort zone. —D.M.

Medical Care Administration

International Development of Occupational Medicine. S. Forssman.* Indust. Med. & Surg. 88:465 (Oct.) 1959. (*Professor or Industrial Medicine, University of Stockholm, Sweden.

Some knowledge of health risks at work existed more than 1,000 years ago in many countries. The works of Hippocrates, Galen, Ramazzini, and Linnaeus contain reports on occupational diseases and on health hazards at work. When industrialization started at the end of the 18th century in England, the increased risk to workers' health was obvious to physicians and laymen, The first law on workers' protection was passed in England in 1833. Accident prevention, the improvement of general hygiene at work, including ventilation and lighting, legislation on workers' protection, hours of work, employment of women and children, and organization of factory inspectorates were the dominating trends in most industrial countries during the 19th century.

From 1935, activities in the field of occupational health were also directed toward the general health of the worker. It was pointed out that accidents and occupational diseases only constituted a minor aspect of workers' health. The experience gained in industrial-health services has shown the increasing importance of mental health and human relations in industry. In France in 1946, legislation was introduced whereby occupational-health service was rendered compulsory for all places of employment. In the Netherlands, similar legislation has recently been introduced. In Soviet Russia health services are compulsory in industry. In the United States, United Kingdom, and many other geographic units, the organization of industrial-health services is voluntary, but there are special regulations for industries with certain health hazards. In Norway and Sweden, industrial-health services are on a voluntary basis but are based on an agreement between employers' organizations and trade unions.

Although medical care is not a part of occupational health, it might sometimes be practical to arrange for some medical care to be given by industrial-health services. The definition of health must be wide, including not only freedom from sickness but a state of complete physical, mental, and social well-being.

On the basis of developments in the last 50 years, one may foresee some future trends. Automation will create problems because of increased mental demands and decreased physical demands on the worker. The preference for younger workers to fill these new jobs will create a problem of replacing and retraining workers 40 years and above. The use of atomic energy will create many problems. Suitable plans for organizing industrial-health services for groups of small firms must be further developed. Special health problems connected with the rapid industrialization of less industrialized countries must be emphasized at the national and international levels. —A.B.

Medicine and Society. A. Heckscher.* New England J. Med. 262:19 (Jan. 7) 1960. (*Twentieth Century Fund, New York City.)

The doctor in solo practice dealing on a fee-for-service basis with the individual patient is a social convention, and like all social conventions is subject to reexamination, to development, and to change. This relationship between the doctor and the patient, in its ethical concepts and ideology, is an outgrowth of the 19th century.

The ethics reflect the prevailing idea of individualism and commercialism. There was a growth of professional standards that put service above personal gain and made it possible for the doctor to attain a disinterested attitude in treating his patients. The ideology assumed that the cost of sickness was something the patient bore alone out of his own resources, and whether he got well or not was up to himself, with no interest of the community involved.

Doctors are aware of the revolution that has overtaken the science of medicine. No less a revolution has taken place in the organization and basic assumptions of the social order. The community has taken on more importance. One knows the individual cannot exist today apart from the social context that gives substance to his desires and direction and stability to his impulses. Two manifestations of group life have played a significant part in changing attitudes toward health and the organization of medical care: the grim phenomenon of modern war and the growing strength of labor unions.

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The need of modern medicine is plainly for some institution that stands between the office of the individual physician and the hospital. Group practice seems to provide one answer. What they are doing seems in tune with the values of the time, with the state of present-day medical science, and with the needs of their profession. —A.B.

Medical Program of Welfare and Retirement Fund of the United Mine Workers of America. W. F. Draper.* J. A. M. A. 172:33 (Jan.) 2) 1960. (*United Mine Workers of America Welfare and Retirement Fund, Washington, D. C.)

Adequate medical care for the miners and their families was, for the most part, unobtainable prior to the establishment of the fund. There was virtually no choice of physician by the people who are now its beneficiaries. Choice was limited to the camp physician employed by the company, whom the miners paid for services received.

In many communities, the fund now pays any physician whom a beneficiary may choose. In other communities, he has a choice from among a majority of the physicians who desire to serve beneficiaries. They may see any one of a large number of specialists, even to the extent of being transported to one or another of the great medical centers of the country. More than 7,000 physicians were paid by the fund in 1958. The relationships with most of the physicians in the coal-mining area have always been cordial and satisfactory and continue to be so. They have provided high-quality care for the miners and their families. —A.B.

Can Blue Cross Save Its Life? F. S. Groner.* J. Am. Hosp. A. 34:44 (Jan. 1) 1960. (*Baptist Memorial Hospital, Memphis, Tenn.)

Life or death is the challenge facing Blue Cross in the next decade. Blue Cross is a community mechanism designed to obtain for the public the best hospital care at the best price. A quarter of a century ago, it was an accepted fact that the sick poor in the country were receiving care but that the middle class citizen was unable to finance adequate medical care and hospital service. To a marked degree, Blue Cross has solved their problem, but other problems have evolved.

Our society assumes that every person has an inalienable right to hospital care when needed. Since hospitals as a group cannot deny this care, the social philosophy exemplified by Blue Cross is a logical one. Blue Cross is able to pay a larger percentage of its income in hospital benefits than is commercial insurance. One of the goals of Blue Cross and the hospitals should be the achievement of a basis of reimbursement that can be rationally supported, understood, and defended.

To achieve a marked degree of success in the sale of a product or service, one must create and maintain a nationwide appeal. This applies to Blue Cross. It must be presented as a nationwide product in order to reach the maximum number of potential consumers. Its survival depends upon its presentation as a national product. —A.B.

Clinical Toxicology

Cantharidin Poisoning. W. W. Oaks,* J. F. DiTunno, T. Magnani, H. A. Levy, and L. C. Mills. A.M.A. Arch. Int. Med. 105:574 (April) 1960. (*Departments of Medicine and Pathology, Hahnemann Medical College, Philadelphia)

Two cases of acute cantharidin poisoning are reported. One patient ingested approximately 175 mg of cantharidin, and the second ingested approximately 75 mg of the material. Both patients experienced burning of the lips and mouth, followed shortly by abdominal pain and nausea. One patient vomited bright red blood. Both patients developed hematuria, and renal biopsies confirmed extensive renal involvement. Liver biopsy in one case and liver function studies in both cases demonstrated hepatic involvement. Electrocardiograms in both cases revealed abnormal patterns. Both patients recovered satisfactorily with supportive treatment. The report includes a review of previously reported cases and discusses in detail the pathological abnormalities and the principles of management of importance in cantharidin intoxication. —A.D.

Effect of D,L-Penicillamine on the Urinary Excretion of Copper and Calcium in Hepatolenticular Degeneration (Wilson's Disease). R. B. Litin,* N. P. Goldstein, R. V. Randall, M. H. Power, and G. R. Diessner. Neurology 10:123 (Feb.) 1960. (*Mayo Clinic and Foundation, Rochester, Minn.)

The authors describe a study of the effects on urinary calcium and copper excretion of the oral administration of D,L-penicillamine in five patients with Wilson's disease and in three healthy men. Urinary copper and calcium excretions were measured for a control period of three days and for a treatment period of three days. Dosage of D,L-penicillamine was 1,500 mg per day by mouth. Daily intake of calcium and of copper were estimated by chemical analysis of an aliquot of a 24 hour diet. In the group of healthy men, urinary excretion of copper was increased 13 to 35 times during the three-day period of treatment with D,L-penicillamine as compared to the three-day period immediately preceding the treatment. The urinary calcium excretion was not altered significantly by the treatment. In the group of patients with hepatolenticular degeneration, urinary excretion of copper was increased 4 to 17 times during the three-day period of treatment with D,L-penicillamine as compared to the three-day period immediately preceding the treatment. As with the healthy men, the urinary calcium excretion was not altered significantly by the treatment. Inasmuch as the urinary copper excretion of the patients with hepatolenticular degeneration

exceeded significantly the total of control period excretion level and dietary copper intake, it is most likely that D,L-penicillamine is effective in mobilizing copper from the tissues of such patients. —A.D.

The Present Status of Dental Research in the Study of Fluorides: Summary of Report. F. A. Arnold.* A.M.A. Arch. Indust. Health 21:308 (April) 1956. (*National Institute of Dental Research, National Institutes of Health, Public Health Service, United States Department of Health, Education and Welfare, Bethesda, M.D.)

Fluoridation of communal water supplies is the method most commonly used in the United States for providing fluorides for the prevention of tooth decay. Over 1,500 communities with a combined population of more than 32,000,000 are involved. In a survey conducted in Grand Rapids, Mich., the caries rate in the deciduous teeth of children 7 years old prior to fluoridation was slightly greater than six per child, whereas 10 years after fluoridation the rate dropped to slightly more than three per child. The rate per child for caries in the permanent teeth was less after fluoridation than before fluoridation, with a difference of approximately four fewer cavities at age 12 and three fewer at age 16. No cases of dental fluorosis considered to be noncosmetic could be found.

Most water-treatment plants use sodium fluoride, sodium silicofluoride, fluosilicic acid, or ammonium fluosilicate. In recent years the last has been preferred, but favorable reports concerning the use of calcium fluoride may change this preference. Topical applications are of value especially in areas where fluoridation of public water supplies is not feasible. The claims of increased effectiveness for stannous fluoride need further substantiation. The use of fluoride supplements to the diet involves special problems, requires daily supervision, and should reach children during the period of formation of the teeth. The value of utilizing dentrifices that contain fluorides has not been established conclusively. —L.H.M.

The Metabolism of Fluorides in Man. Edward J. Largent.* A.M.A. Arch. Indust. Health 21:318 (April) 1960. (*Reynolds Metals Co., Reynolds Metals Building, Richmond 18, Va.)

In man, the absorption of fluoride from the alimentary tract is quite effective. Sodium fluoride and calcium fluoride in solution are absorbed nearly completely (96%-97%). Calcium fluoride, bone meal, cryolite, and rock phosphate, when administered as solids, yield their fluoride for absorption approximately 62%, 32%, 77%, and 87% respectively. Approximately half of the amount of simple fluoride salts absorbed after ingestion is excreted in the urine. The rest is retained in the body, primarily in the skeleton. Small amounts of unabsorbed fluoride appear in the feces. Fluoroborate is absorbed readily and excreted as such in the urine. Healthy persons achieve a balance between input and output of fluoride when the diet contains between 0.4 and 0.8 mg per day. Under conditions of "abnormally" high intake and absorption, the rate of retention of fluoride is influenced by the magnitude of the increased absorption and by the amount of fluoride that has accumulated in the body. Stored fluorides are released slowly, and at a progressively diminishing rate when the level of fluoride intake is reduced. Fluoride is excreted in sweat, and the concentration in the sweat varies directly with the rate of intake and absorption. Fluorides are absorbed and excreted rapidly after exposure to HF in the atmosphere. Similar findings have been reported by Collings when subjects were exposed to finely divided rock phosphate. —L.H.M.

Noise and Hearing

Equal-Loudness Contours for Octave-Band Noise in a Diffuse Field (Kurven gleicher Lautstärke mit Oktav-gefiltertem Rauschen im diffusen Schallfeld). L. Cremer,* G. Plenge, and D. Schwarzl. Acustica 9:65 (March) 1950. (*Heinrich-Hertz-Institut für Schwingungsforschung, Berlin-Charlottenburg, Germany.)

Equal-loudness contours were determined for octave-band noises, using 27 normal-hearing observers. The noises were generated by means of a loudspeaker in a reverberant room, in contrast to previous studies of equal-loudness relations, which have generally involved earphone presentation. The intensity of each octave band in the range from 100 to 12,800 cps was adjusted to give the same loudness as a reference third-octave-band noise of 900-1200 cps at levels of 50, 60, 70, 80 and 90 db SPL (sound-pressure levels). The 5 resulting equal-loudness contours are essentially parallel, so that a generalized equal-loudness contour that holds for loudness levels of 50 phons and above can be drawn. If the SPL of the octave band 800-1600 cps is L db, then the levels of the other octave bands for equal loudness are as follows: 100-200 cps, L+8; 200-400 cps, L+6; 400-800 cps, L+3; 1600-3200 cps, L–6; 3200-6400 cps, L–8; and 6400-12800 cps, L–10.

NOTE: Although the authors conclude that, on the average, the function shows a downward slope of 3 db per octave, the departures from this average—especially the 6-db difference between 800-1600 cps and 1600-3200 cps—are statistically significant.) —W.D.W.

Noise Control for Offices. L. N. Miller* and I. Dyer. Noise Control 3:70 (March) 1957. (*Bolt, Beranek and Newman Inc., Cambridge, Mass.)

Some typical office-noise problems and solutions for offices located near production machines and mechanical-equipment spaces are discussed with emphasis on the engineering procedures which are available for application to these problems.

Three types of noises which are frequently encountered in office-noise problems are discussed:

Abstracts

(1) industrial noise, (2) vehicular noise, and (3) air-conditioning-system noise. The examples used are reasonably representative of those general types of noise. The same general procedure used in studying and solving typical noise problems was followed. This procedure includes (1) determination of the true causes of the complaint; (2) estimations of the noise conditions that would be considered satisfactory for the particular office based on the functional uses and needs of the office; (3) measurement of the noise level and, when necessary, the vibration level in the office with the offending noise maker on and off; (4) calculation of the amount of noise reduction required for the office, based on the noise measurements and the noise level criteria; and (5) design of noise control schemes to satisfy the noise-reduction requirements. The author then demonstrates the application of these procedures in the following five specific examples of office noise problems: (1) executive office, (2) industrial business office, (3) business office, (4) shop inspection area, and (5) another executive office. Schematic sections showing structural characteristics and noise-control treatment for the five examples are given. The measured noise and/or vibration levels and the recommended criterion levels for each example are given in eight graphs.

The authors point out that there is no fixed or stereotyped solution to noise problems and that each problem is solved on the basis of the amount of noise reduction required and the analysis of noise and/or vibration levels along the various paths from the source to the receiver. —R.G.H.

Hearing Losses of Personnel Exposed to Impulse and Steady State Noise. J. L. Fletcher.* U. S. Army Medical Research Laboratory Report 355, (Aug. 11) 1958. (*Experimental Psychology Department, U. S. Army Medical Research Laboratory, Fort Knox, Ky.)

The army soldier may be exposed to steady-state noise (produced by tanks and other vehicles) from 90 to 129 db and to impulse noises (from firing on the ranges) ranging from 100 db to more than 150 db. This report is a comparison of the hearing losses of personnel exposed to one or the other of these noises. Audiograms were carefully collected on 105 firing-range operators who were selected as having been exposed primarily to impulse noise. Sixty persons primarily exposed to steady-state noise were selected from the Ordnance and Automotive Department. Subjects were separated on the basis of time on the job into three categories: 1 to 39 months, 40 to 79 months, and exceeding 80 months. No attempt was made to equate the total energy in the exposures that the subjects had experienced. The median age for the subjects exposed to impulse noise was 35 years, and for those exposed to the steady-state noise it was 38 years. The results indicate that hearing losses for the two types of exposures are essentially identical for the 1- to 39- and 40- to 79-month time-on-job categories. Hearing losses at 2000, 4000, and 8000 cps for subjects in both noise-exposure groups were significantly greater in the 1- to 39-month category than in those with 40- to 79-months exposure. The author makes the personal observation that this might be because the 1- to 39-month group may include many who will later transfer to other jobs because they cannot tolerate the noise.

The hearing losses for those exposed to steady-state noise on the job for 80 months or longer tend to be larger than those for subjects exposed to impulse noise on the job for the same length of time. The need for further research work to establish criteria for hazardous exposure and to determine if and where workers should be rotated from their job is recommended. —R.G.H.

Some Variables in Audio Spectrometry. R. W. Benson* and I. J. Hirsh. J. Acoust. Soc. America 25:499 (May) 1953. (*Central Institute for the Deaf, St. Louis, Mo.)

Various measurements of the long-time average spectrum of speech are reported with the purpose of pointing out the roles of several variables. The authors examined the following four sources of variability: (1) the size of the bands used in analysis (octave, half-octave, equal-mel); (2) the type of speech material (technical material, news, and a test sentence); (3) the length of the speech sample (30-, 60-, and 90-second durations); and (4) the individual talkers. Three different sampling times of three different types of speech material, spoken by five young men and five young women, were analyzed using bandwith intervals. No significant differences in the long-time average spectra were found among the three types of speech material (technical material, news, and a test sentence). There were no significant differences in the three different sampling times of 30, 60, and 90 seconds. The long-time average spectra for 90-second samples of technical and news material and for the 4-second test sentence appear to be equivalent. The variability among these three types of material was no greater than the variability among three successive 30-second samples of the same material (news). It is also concluded that the minimum sample time required for a long-time result is, at most, four seconds and is probably considerably less. The authors point out that much of the variability among talkers that has been reported previously appears to be attributable to the over all speaking level and not to the shape of the long-time average spectrum. The octave-, half-octave-, and equal-mel-interval analysis all appear to yield the same results. The only important difference between male and female speech appeared in the octave band 75-150 cps, where men were approximately 20 db higher. The authors also discuss the meaning of "overall level" and they describe a relatively simple system for obtaining these measurements. —R.G.H.

About the Authors

► CLYDE C. GREENE JR., M.D., was born in Charlotte, N. C. He graduated from Wake Forest College (North Carolina) in 1937, and from Jefferson Medical College, Philadelphia, in 1941. He interned at Jefferson Hospital until serving in the U.S. Army Medical Corps from 1942 to 1946. After World War II, Dr. Greene completed his residency at Stanford University Hospital in San Francisco.

Dr. Greene has been associated with The Pacific Telephone & Telegraph Company since 1947. He is General Medical Director in the Company's general headquarters, in San Francisco.

In addition to his duties with Pacific Telephone & Telegraph, Dr. Greene is Assistant Clinical Professor of Medicine at Stanford University School of Medicine. He is a member of Alpha Omega Alpha, Industrial Medical Association, American Academy of Occupational Medicine, and the American Society of Internal Medicine. He is the senior author of our lead article this month, "A Study of Mass Influenza Inoculation in a Large Industry."

► GLEN T. BEAVER is a Californian and an engineer by profession. He received a B.S. degree in Electrical Engineering from the University of California in 1929. After graduation, he joined The Pacific Telephone & Telegraph Company in an engineering capacity. For the past 10 years, Mr. Beaver has been involved in mathematical-statistical, public opinion measurement, and social science research activities converging all phases of the company's operations. He is co-author of the article in this issue, "A Study of Mass Influenza Inoculation in a Large Industry."

► DAVID I. ABRAMSON, M.D., is author of the dissertation, "Differentiation of Venous Thrombosis of the Lower Extremities," one of the highlights of IMA's Annual Meeting in Chicago in April, 1959. Dr. Abramson is Professor and Head of the Department of Physical Medicine of the University of Illinois and chief of the clinical services in this specialty at the University's Research and Educational Hospitals.

He is the author of 87 articles and two books on peripheral vascular physiology and diseases, and cardiology. From this substantial background of literary experience comes the engagingly written article in the present issue.

Dr. Abramson's career began in New York, continued in Cincinnati, and now flourishes in Chicago. He graduated in medicine from Long Island College of Medicine in 1929 and served a rotating internship at Bushwick Hospital, Brooklyn. He was thereafter for a period of six years an instructor in the Department of Physiology and Pharmacology of his alma mater, and for one year a fellow in cardiovascular research at Mount Sinai Hospital, New York.

Dr. Abramson moved to Cincinnati in 1937, and for six years filled various posts: Director of Cardiovascular Research, May Institute for Medical Research; Director of the Department of Electrocardiography, Jewish Hospital; and instructor in the Department of Pharmacology at the University of Cincinnati.

During the war he served in the cardiac diseases ward of O'Reilly General Hospital and was Section Chief of the Peripheral Vascular Center, Mayo General Hospital. He went to Chicago after the war, and progressed through various appointments in the Department of Medicine at the University of Illinois College of Medicine to his present professorship. DR. ABRAMSON'S additional clinical activities include appointments at Michael Reese, Mount Sinai, and Hines Veterans' Administration Hospitals.

► LOWELL G. WAYNE, M.D., was born in Washington, D.C., in 1918 and has been a Californian since 1920. His boyhood was spent in San Francisco. He graduated, *cum laude*, with a B.S. degree from the College of Chemistry, University of California, at Berkeley in 1937. He then spent two years with Shell

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About the Authors

Development Company before returning to the University of California, this time as a graduate student in agricultural chemistry at Davis.

Dr. Wayne served during World War II in the Navy's Industrial Hygiene Program. This involved an industrial hygiene course at Harvard School of Public Health and duty as an Industrial Hygiene Engineering officer, Medical Services Corps, seeking ways to safeguard the health of civilian workers at navy industrial shore establishments, principally by control of toxic contaminants in the environment.

After the war, he studied at the California Institute of Technology, receiving the degree of Ph.D. in Chemistry in 1949 for research on the oxides of nitrogen. This was followed by a postdoctoral research fellowship at the University of Colorado and three years of research in the chemistry of catalytic cracking of petroleum as a Fellow of Mellon Institute for Industrial Research in Pittsburgh, Pa.

Since returning to California, Dr. Wayne has been engaged in studies in fog physics for Stanford Research Institute and in industrial hygiene for the University of California. He joined the Air Pollution Control District as a photochemist in the Research Division, in May, 1956.

He is a member of Sigma Xi; American Association for the Advancement of Science, Adult Education Association, and American Industrial Hygiene Association, and in 1956 was Chairman of the Los Angeles Chapter of the Federation of American Scientists. He is also a member, Air Pollution Control Association.

Dr. Wayne is senior author of the informative article in this issue, "Relative Potentials of Common Organic Solvents As Precursors of Eye-Irritants in Urban Atmospheres."

► JAMES A. ORCUTT, M.D., is coauthor of the article in this issue, "Relative Potentials of Common Organic Solvents as Precursors of Eye-Irritants in Urban Atmospheres." After receiving a bachelor's degree in biochemestry at the University of Chicago in 1939, he completed work for a master's degree in the following year at the same institution. This was followed by research in chemistry of packinghouse processing and cooking, sponsored by the American Meat Institute, and by studies in high altitude sickness, conducted for the United States Air Force.

He moved to the University of Rochester in 1944, where he served as an instructor in pharmacology, and in the course of the next two years completed work for the Ph.D. degree.

Dr. Orcutt served as Chief, Division of Pharmacology, Eaton Laboratories, Inc., from 1946 to 1950 and was then associated with Riker Laboratories, Inc., for two years. He took his present position with Air Pollution Control District, County of Los Angeles, in 1956. He is the author of numerous articles in the fields of biochemistry, physiology, and pharmacology.

► ROGER F. LAPHAM, M.D., is Medical Director of General Foods Corporation. A native of Utica, New York, Dr. Lapham received the A.B. degree from Syracuse (New York) University in 1928, and four years later from the same institution received the M.D. degree, *cum laude*. This was followed by two years of internship at the New York Post Graduate Hospital, which gave emphasis to pathology, pediatrics, and internal medicine. He thereafter practiced as an internist in New York until 1954, when he assumed the medical directorship of General Foods on a full-time basis.

Dr. Lapham is the author of two published books: "Patient and Disease" (Oxford University Press, 1937) and "It's in Your Power" (Derell, Sloane and Pierce, 1949).

Dr. Lapham is a member of various local and national medical organizations, including New York Academy of Medicine, American Heart Association, American Association for Advancement of Science, and IMA. He is the author of "Retirement—An Orientation and a Method of Industrial Approach."

—EDITOR

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People and Events

► GERALD DALE DORMAN, M.D., Medical Director of the New York Life Insurance Company, New York City, has been elected to the Board of Trustees of the American Medical Association. The election by the House of Delegates took place at the Association's 109th annual meeting held at Miami Beach, Florida, in June. He succeeds LEONARD W. LARSON, M.D., Bismarck, N.D., pathologist, who was chosen President-Elect and who served many years on the board.

DR. DORMAN has been an AMA delegate from the Medical Society of the State of New York for the past six years and is presently serving the AMA as chairman of the Committee on Workmen's Compensation, as Eastern co-chairman of the Physician Committee on Radio and Television, and is a member of the Medical Affairs and Insurance and Prepayment Plans committees.

DR. DORMAN was born in Beirut, Lebanon, where he lived for 17 years before coming to the United States. He attended Harvard University and received a bachelor's degree in 1925. In June, 1929, he received his medical degree from Columbia University. He interned in surgery at St. Luke's hospital, New York City, and was in the private practice of surgery in that city until 1942 when he entered the Army as a field surgeon serving with the second evacuation hospital in Europe. He is now active in the reserve as Colonel in Command of the 307th General Hospital.

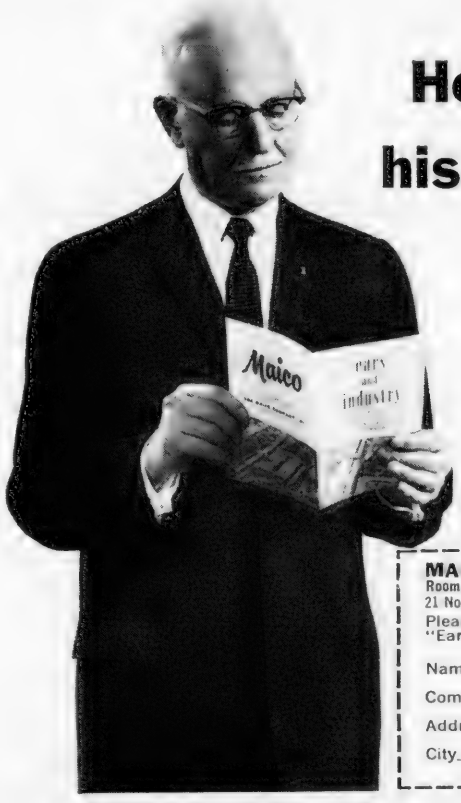
DR. DORMAN is a Fellow of the Industrial Medical Association, a member of the New York Academy of Medicine, a Trustee of the Bamascus College in Syria, a Director of the New York City Cancer Committee and Chairman of its Research and Grants Committee and a consultant to the National Planning Committee on Health and Medical Care for the 1961 White House Conference on Aging.

► RICHARD E. WALTERS, M.D., has been appointed by the Granite City Steel Company, Granite City, Ill., as its first full-time Medical Director. He succeeds WILLIS W. BOWERS, M.D., who has served as part-time Medical Director since 1939. He resigned to devote more time to his private practice.

Gerald D. Dorman, M.D.

Richard E. Walters, M.D.

DR. WALTERS was Medical Director of the Cummins Engine Company, Columbus, Ind., from 1956 until his present appointment. He received his bachelor's degree from the University of Wichita in 1947 and his M.D. degree from the University of Kansas in 1951. He was a flight surgeon in the U.S. Air Force at Waco, Texas, from 1953 to 1955. He then became a resident in surgery at the Cincinnati College



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of Medicine and Christ Hospital, where he remained until joining Cummins. He is a member of the Medical Advisory Council of the Mid-Indiana Association of Industrial Nurses, and a member of the Industrial Medical Association.

At Granite City Steel, he will administer the entire medical department with emphasis on a preventive medicine program. He will also participate in the American Iron and Steel Institute's Committee on Industrial Medicine, as well as in local and national industrial health programs.

► CHESTER L. SAMUELSON, M.D., joined the Ohio Oil Company on July 1 to head the Company's medical department, succeeding JOHN H. HEGE, M.D., who formed the medical department for Ohio Oil in 1957. DR. HEGE resigned to complete advanced training in psychiatry and is now associated with The Mental Health Institute in Independence, Iowa.

Chester L. Samuelson, M.D.

For the past eight years DR. SAMUELSON has been Medical Director of Socony Mobil Oil Company's Paulsboro, N.J., operations. Previously he was Medical Director of the Harrison Radiator Division of General Motors Corporation, Lockport, N.Y., and also was formerly associated with the medical department of the Endicott Johnson Corp.

DR. SAMUELSON received his M.D. degree from the University of Iowa Medical School in 1937. After his internship at Receiving Hospital in Detroit, Mich., he was in private practice for two years. Since that time, he has attended several postgraduate schools on specialized problems of industrial medicine. He is a Fellow of the Industrial Medical Association.

► DOUGLAS H. K. LEE, M.D., has been appointed chief of the research headquarters of the Occupational Health Program, Public Health Service, U. S. Department of Health, Education, and Welfare, at Cincinnati, Ohio. In his new position, DR. LEE will be responsible for directing technical research and field studies of occupational health problems and professional and technical consultation services to State agencies, labor, and industry.

Prior to his association with the Public Health Service, DR. LEE had been in charge of the research program of the Quartermaster Corps, Department of Army. Previously, he was Dean of the Faculty of Med-

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icine and Head of Department of Physiology at the University of Queensland in Brisbane, Australia, and later on the faculty at Johns Hopkins University. His major research interests have dealt with the effect of climate on man and animals and related studies on clothing, housing, and production.

He has also served as consultant to the Food and Agriculture Organization of the United Nations, the Bureau of Dairy Industry of the U. S. Department of Agriculture, and the U. S. Department of Defense. In addition to the United States and Australia his investigations have covered New Guinea, Malaya, Venezuela, and India.

Born in Bristol, England, DR. LEE received his education in England and Australia. A graduate of the University of London and the University of Sydney, he holds degrees in medicine and tropical medicine. DR. LEE is a fellow of the Royal Australasian College of Physicians and a member of the Society of the Sigma Xi, the Physiological Society of Great Britain, and the American Physiological Society. He is the author of numerous publications.

► RITA PACKER, Assistant Managing Director of the Industrial Medical Association, was recently elected Secretary and Treasurer of the Conference of Medical Society Executives of Greater Chicago. This group meets monthly to discuss the common problems of medical society operation. The organization has a membership of approximately 50 persons representing the many medical societies located in the city.

► Industrial Medical Association of Pittsburgh held its semi-annual scientific meeting on May 30 at the Reliance Electric and Engineering Company offices in Cleveland, Ohio. Arrangements for the meeting were made by WILLIAM W. MARKLEY, M.D., physician in charge of medical services at Reliance.

DANIEL C. BRAUN, M.D., of the United States Steel Corp., and President-Elect of the Association, presided over the morning session which was devoted to a general discussion entitled "Tangible Returns from Health Maintenance."

DANIEL V. DOUGHERTY, M.D., of the Ford Motor Company, and President of the Association, presided over the afternoon session which included talks on "Skin Grafting of Burns" and "Safety in Handling of Toxic Propellants."

► SALLY KREGER, R.N., of Paramount Pictures Corp., has received the 1960 Award of Merit in Industrial Nursing given by the Public Health Association of New York City. This award was presented by SYLVAN FURMAN, President of the Board, to MRS. KREGER for her outstanding contributions over the past two years in her capacity as chairman of the Education Committee of the Greater New York Association of Industrial Nurses, Inc. With the assistance of her committee, she has developed and carried out an effective program to introduce the concepts and practice of industrial nursing into the curriculum of nursing schools in the New York area.

► The name of the AMA Archives of Industrial Health has been changed to Archives of Environmental Health, with three subtitles: Preventive Medicine, Industrial Health, and Aerospace Medicine.

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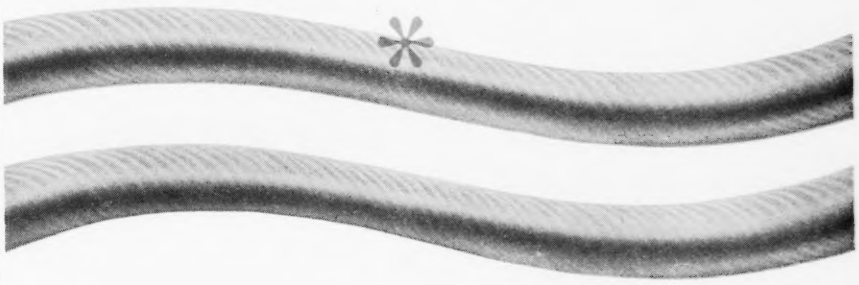

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People and Events

The new name revises the basic concept of the mission of the journal by recognizing a wider horizon, according to JOHN H. TALBOTT, M.D., Director of AMA Division of Scientific Publications. The July, 1960, issue was the first bearing the new name.

► American Conference of Governmental Industrial Hygienists announces the publication of a "Guide to Records for Health Services in Small Industries," which was developed in response to a need for specific guidelines on health records in industry. This 8½ by 11 inch manual, consisting of 32 pages of text and suggested forms, is especially designed to assist in developing or improving record systems for employee health services in small industrial or business establishments.

Copies of the Guide are available for $1.00 from the Secretary-Treasurer of the organization, c/o Occupational Health Field Headquarters, Public Health Service, U.S. Department of Health, Education and Welfare, 1014 Broadway, Cincinnati 2, Ohio.

Manfred Bowditch

► MANFRED BOWDITCH, Director of Health and Safety of the Lead Industries Association since 1948, died on June 29, apparently of a heart attack. He was 69 years old.

MR. BOWDITCH previously was field director of the Saranac Laboratory and Director of the Massachusetts Division of Occupational Hygiene. There he conducted experiments in methods of eliminating or curtailing the danger from silica dust.

Born in Dresden, Germany, of American parents, he was brought to the United States as a child. He graduated from Harvard in 1912 and later became an instructor in industrial hygiene at the Harvard School of Public Health, and Professor of Industrial Hygiene at Tufts Medical School. In 1925 he became a hygienist with the General Electric Company, and is believed to have been the first full-time industrial hygienist employed by any United States industry.

MR. BOWDITCH was a member of the American Public Health Association, a charter member and director of the American Industrial Hygiene Association and a member of the Committee on Toxic Dusts of the American Standards Association. He also belonged to the Air Pollution Control Association, the American Conference of Governmental Industrial Hygienists, the American Association for the Advancement of Science, the National Safety Council and other organizations in his field. He had lectured extensively and written many articles on industrial health and safety.

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